PA NT COOPERATION TREAT

6

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To

Assistant Commissioner for Patents United States Patent and Trademark Office Box PCT Washington, D.C.20231 ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 19 August 1999 (19.08.99)

International application No. PCT/GB99/00055

International filing date (day/month/year) 08 January 1999 (08.01.99)

Applicant's or agent's file reference P003839WO RWP

Priority date (day/month/year)

12 January 1998 (12.01.98)

Applicant

O'NEILL, Graham et al

1.	The designated Office is hereby notified of its election made:
''	<u> </u>
	X in the demand filed with the International Preliminary Examining Authority on:
	03 August 1999 (03.08.99)
	in a notice effecting later election filed with the International Bureau on:
2.	The election X was was was not
	made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).
•	

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Lazar Joseph Panakal

Telephone No.: (41-22) 338.83.38

Facsimile No.: (41-22) 740.14.35

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:		(11) International Publication Number:	WO 99/35882
H04R 25/00	Al	(43) International Publication Date:	15 July 1999 (15.07.99)

(21) International Application Number:

PCT/GB99/00055

(22) International Filing Date:

8 January 1999 (08.01.99)

(30) Priority Data:

9800585.3 9816351.2

12 January 1998 (12.01.98)

GB 27 July 1998 (27.07.98)

(71) Applicant (for all designated States except US): IMPERIAL COLLEGE OF SCIENCE, TECHNOLOGY & MEDICINE [GB/GB]; Sherfield Building, Exhibition Road, London SW7 2AZ (GB).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): O'NEILL, Graham [GB/GB]; 15 Brynmorlais Street, Penydarren, Merthyr Tydfil CF47 9YE (GB). GERMANOVIX, Walter [BR/BR]; Apartamento 1102, Rua Pio XII, 731, CEP-86020-311 Londrina, PR (BR). TOUMAZOU, Christofer [GB/GB]; 4 Hurst Lane, Cumnor Hill, Oxford OX2 9PR (GB).
- (74) Agent: PRATT, Richard, Wilson; D. Young & Co., 21 New Fetter Lane, London EC4A 1DA (GB).

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

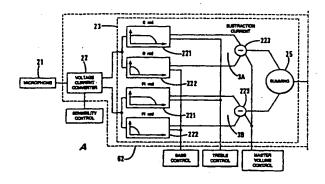
With international search report.

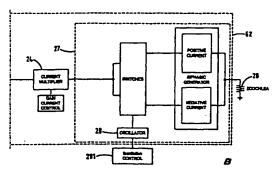
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: AUDIO SIGNAL PROCESSORS

(57) Abstract

An audio signal processor includes a tone control (23). The tone control comprises two low-pass filters (221, 222) operating in current-mode and a subtractor (223) which subtracts the output currents of the filters to produce a band-pass characteristic. Each filter is a tuneable log-domain current-mode filter comprising MOS transistors operating in weak inversion. The tone control is useful in audio signal processors, hearing aids and single-channel and multi-channel Cochlear implants.





FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

АL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
ΑU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
ΛZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD ·	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of Americ
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
Cl	Côte d'Ivoire	, KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		•
CN	China	KR	Republic of Korea	PT	Portugal		•
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DΕ	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

17/PRTS

09/600206 534 Rec a PCT/PTC 12 JUL 2000

WO 99/35882

5

15

20

25

30

PCT/GB99/00055

Audio Signal Processors

embodin

Field of

prostheti

processo

signal pi

udio signal processors. Preferred
dio signal processors for use in aural
the invention concern audio signal
embodiments of the invention concern audio
plants. Yet further embodiments concern

hearing aids and Cochlear Implants.

Summary of the Invention

particular, Hearing Aids,

provide considerable help for most individuals with ing loss. Whilst modern aids are small and consume further reduce the size and power consumption of sirable to produce a simple circuit with reduced cost

tor a nearing aid. Such a simple circuit would also be applicable to other audio signal processing tasks.

Also, a pre-requisite of all modern hearing-aids is a method of adjustment of the intensity-frequency content of the output of the device in order to compensate appropriately, across the frequency range, for the individual's pattern of hearing loss. For any one frequency, or band of frequencies, this includes device adjustment for both the 'threshold' level of hearing and the 'uncomfortable' loudness level; the difference between these two values being known as the 'dynamic range'. Tone controls are known for various audio applications: see [1], [2] and [3]. In conventional hearing-aids tone control is accomplished by potentiometer-controlled low and high-pass analogue filtering in combination with 'output compression'.

According to one aspect of the invention there is provided an analogue signal processor the analogue processor having an input for receiving an audio signal, an output for delivering a processed audio signal to an audio output transducer, and log-domain filter means comprising MOS transistors operating weak inversion for processing the audio signal. The audio signal is preferably a current signal.

The invention also provides a hearing aid comprising the analogue signal processor of the said one aspect of the invention.

Thus, the invention provides a very low power consumption by virtue of the MOS transistors operating in weak inversion.

5 Cochlear Implants

10

15

20

25

30

Hearing aids are of little help where the deafness is 'profound', that is average loss is greater than about 96dB in both ears. In such cases an electronic device, surgically implanted in the inner-ear, can provide electrical stimulation to the nerve of hearing, giving the individual a degree of hearing sensation. In some cases open-set speech discrimination is possible, e.g. understanding a telephone conversation.

A Cochlear Implant takes-in environmental sounds, including speech, and converts this into an electrical signal which, by way of for example an implanted wire electrode array, stimulates discrete regions of the inner-ear Cochlea.

From the mid 1980s to around 1990, patients considered suitable for a Cochlear Implant were mainly adults who had, before their deafness, acquired speech and language. They were old enough to understand the implications regarding surgery and post-operative rehabilitation and, having past experience of speech and language, there was considerable potential for a return to an oral communication environment. Gradually, as clinicians around the world became more aware of the benefits of the Cochlear Implant, the focus of attention turned to the profoundly deaf child. From around 1990 onwards, an increasing number of children received a Cochlear Implant and, in the main, the results have been encouraging.

Because of the success of Cochlear Implants it is expected that, in the future, these devices will even be considered for patients having a greater amount of residual hearing.

Although there have been proposals to provide analogue circuits for use in Cochlear Implants (see [6],[9]) according to the current knowledge of the applicants at present all Cochlear Implants are actually implemented with Digital Signal Processors. Present devices, regardless of manufacturer, are based upon digital technology, for example standard DSP chips and ASICs. The patient wears an external 'speech processor', about the size of a large match-box. This picks-up and processes

environmental sounds and passes an electrical signal, via a radio-frequency link, to a 'receiving' device implanted in the ear. This internal receiver sends an electrical signal through a long thin multi-electrode array (up to 22 separate electrodes) within the inner turns of the Cochlea. Thus, the Cochlea is electrically stimulated at discrete sites and the result is a perception of sound. The stimulus intensity, delivered to each channel of the electrode array, needs to be programmed 'channel by channel'. This technology has significant advantages of flexibility, with modifications being achievable through software rather than hardware. The use of a Digital Signal Processor (DSP) provides the manufacturer with the ease of using software to alter various parameters which might be thought important in the development of new processing strategies.

It is desirable to provide in a Cochlear Implants a method of adjustment of the intensity-frequency content of the output of the device in order to compensate appropriately, across the frequency range, for the individual's pattern of hearing loss. For any one frequency, or band of frequencies, this includes device adjustment for both the 'threshold' level of hearing and the 'uncomfortable' loudness level; the difference between these two values being known as the 'dynamic range'. With Cochlear Implants, this output shaping has, up to the present time, been performed by channel-by-channel 'programming'.

The Cochlear Implant designs discussed hereinabove are based upon long, multi-channel electrodes, inserted deep within the Cochlea. The multi-channel design can be used to provide tonotopically distributed information from several processing strategies namely:

- i. Continuous Interleaved Sampling CIS
- ii. Feature Extraction or

10

15

20

25

30

iii Analogue compression

Good results, in terms of open-set speech discrimination have been reported, particularly with the CIS and Feature Extraction strategies.

There are disadvantages associated with Cochlear Implants especially multichannel implants:-

i. Deep insertion of long electrodes can cause considerable damage to surviving neuronal tissue in the diseased cochlea. That is, residual hearing, albeit minimal, is destroyed.

- ii. The fitting/programming of current multichannel devices requires channel by-channel adjustment of stimulation levels for both threshold and uncomfortable levels. Considerable expertise is required to programme a 'MAP' which the user feels is the most useful. With current Cochlear Implants, having between 12 and 22 separate electrodes, this 'channel-by-channel' programming is time-consuming, particularly since the implant has to be re-programmed about 3-4 times over the first 12 months after the operation. Some users, even with appropriate counselling, regularly attend for 'reprogramming', over several years, in the hope that one particular 'programme' will result in almost perfect hearing.
- The DSP based technology has significant drawbacks of high power consumption and physical size. With the current digital devices batteries need changing every few (e.g. 1-2) days or even more frequently, and many patients are unhappy about wearing a relatively large speech processor, although smaller 'behind-the ear' digital processors have reached a fairly advanced stage of development.
 - iv. Hardware costs are high (approximately £ 15,000).

10

15

20

25

30

The use of a short electrode, single channel system has been advocated by House [7]. He argues that such a system has advantages over a 'long electrode' design in that-

- i. A short single intra-cochlea electrode will significantly reduce the possibility of damage to residual hearing.
- ii. The system design is simple and relatively inexpensive (about 1/3 the cost of a multichannel system)
- iii. Power consumption is low, and a head-worn processor can be used.
- iv. Fitting/programming is easier and quicker than with multichannel devices.

The articles [6] and [9] disclose an analogue log-domain low-pass filter implemented in MOS technology and having MOS transistors working in weak

inversion. The articles propose the use of such filters in an electronic Cochlear prosthesis.

According to another aspect of the present invention, there is provided an analogue audio signal processor for use in a cochlear implant, the processor comprising:

an input for receiving an audio signal,

5

10

15 .

20

30

an output for delivering a processed audio signal to a cochlear implant electrode, and a tone control circuit for adjusting the intensity-frequency content of the audio signal fed to the output and comprising first and second filters having different low-pass bands and a subtractor for subtracting the output currents of the filters to produce band-pass filter characteristic,

each of the first and second filters being log-domain filters comprising MOS transistors operating in weak inversion.

The audio signal is preferably a current signal.

The invention involves the use of analogue electronics in a way which allows realisation of an extremely small processor with a very low power requirement. Weak inversion or sub-threshold mode of operation of MOS transistors results in an exponential characteristic (or a natural logarithmic characteristic) which is compatible with the exponential characteristic of the Cochlear. Although we envisage the processor being kept external (e.g. behind-the-ear), the invention does, theoretically, allow consideration of a totally implantable device. This is not true of even the most modern developments in digitally-based devices. If the tone control is implanted in the Cochlear, adjustment of the frequency response is performed by wireless remote control. The tone control allows the user for the first time in cochlear implants to control the frequency/intensity content of the audio signal.

According to a further aspect of the invention, there is provided an analogue audio signal processor for use in a cochlear implant prosthesis, comprising

an input for receiving an audio signal,

a plurality of outputs for connection to respective cochlear implant electrodes, for delivering processed audio signals thereto, and

a tone control common to all the outputs for simultaneously adjusting the intensity/frequency content of processed audio signals fed to the said outputs, the tone control comprising MOS transistors operating in weak inversion.

According to a yet further aspect of the invention, there is provided a single channel audio signal processor for use in a Cochlear prosthesis, and including a tone control comprising a log-domain filter having MOS transistors operating in weak inversion, and means controllable by the user of the prosthesis for adjusting the frequency response of the tone control.

According to yet another aspect of the invention, there is provided a multichannel channel audio signal processor for use in a Cochlear prosthesis and including a tone control common to all the channels at least the frequency response of which is controllable by the user.

10

15

20

25

30

We believe that for adults at least, and with the appropriate professional support, giving the user the ability to adjust the tonal quality of their device would be a significant step towards simplifying device re-programming after the initial fitting. We also believe that by this means the user would more readily accept the limitations of the implant and not, as is the case with some, become frustrated with the clinician's attempts at re-programming to reach a quality of sound perception which is, perhaps, for them, unachievable. To this end, our Cochlear Implant design, unlike other current designs, incorporates a 'tone-control', providing easy and rapid frequency shaping of the output. This constitutes a new innovation in Cochlear Implants. Also the use of a tone control common to all the channels of a multi-channel Cochlear Implant allows the instant and simultaneous adjustment of all the channels.

According to yet another aspect of the invention, there is provided analogue multi-channel audio signal processor for use with a Cochlear Prosthesis and comprising

an input for receiving an audio signal,

a plurality of outputs for connection to respective Cochlear Implant electrodes,

a plurality of analogue, signal processing channels coupled to the said input and each comprising a log-domain filter having MOS

10

15

20

30

transistors operating in weak inversion, the channels being coupled to respective ones of the outputs, the intensity/frequency response of each channel being adjustable, and

means for adjusting the intensity/frequency response of each channel.

Thus, a multi-channel audio signal processor for use in a cochlear prosthesis is provided, having a small size and low power consumption.

The adjustment of each filter allows the patient to adjust the processor him or her self. Preferably the adjusting means is a wireless remote control. Preferably the remote control has buttons for selecting respective ones of the channels. Most preferably, the patient adjusts the gain (volume) of the chosen channel between the threshold and uncomfortable levels of sound intensity. The patient may be able to vary filter frequency of a channel in some embodiments. The patient may need the assistance of a skilled technician to guide him or her in the adjustment.

Thus, this aspect of the invention allows the patient to control the processor him or her self (albeit with some guidance from a technician). This simplifies reprogramming after initial fitting and the patient may more readily accept the limitations of the Cochlear Implant

According to a yet further aspect of the invention, there is provided a current mode analogue tone control circuit for use in an audio signal processor, the tone control comprising MOS transistors operating in weak inversion. Such a tone control provides reduced size and power consumption. The audio signal processor may be an aural prosthetic device.

nderstanding of the present invention and to show how the same ffect, reference will now be made by way of example to the 1gs in which:

schematic block diagram of an illustrative hearing aid in invention;

chematic block diagram of an illustrative single channel

Cochlear Implant prosthesis;

8

Figure 3 to 5 are diagrams illustrating the operation of the prosthesis of Figure 2;

Figure 6 is a schematic block diagram of an illustrative multi-channel Cochlear Implant prosthesis;

Figure 7 is a schematic diagram illustrating the operation of a sample interleaving circuit of the prosthesis of Figure 7;

Figures 8A to C are diagrams of an inventive tone control circuit suitable for use in the hearing aid of Figure 1, or the prosthesis of Figure 2 or 6;

Figures 9A and 9B are frequency/amplitude diagrams for the tone control of Figure 8;

Figure 10 is a schematic block diagram of a Hearing Aid or Cochlear Implant according to the invention and having a wireless remote control;

Figure 11 is a diagram of the Voltage to Current converter of Figure 1,2 or 6; and

Figure 12 is a diagram illustrating control of sensitivity;

Figures 13A to D are diagrams of an example of a band-pass filter of the multi-channel Cochlear implant of Figure 6.

Description

5

10

15

25

30

1 an illustrative hearing aid according to the invention voltage to current converter, which is also a compressor, to the invention, a current amplifier 4, and a loudspeaker f an earpiece. The hearing aid operates entirely in the

dynamic voltage range but the ear requires a different, smaller, dynamic range. The compressor 2 compresses the dynamic range and converts the voltage to current. The compressor 2 may also provide sensitivity control controllable by the user. The tone control 3 is controllable by the user and allows adjustment of bass, treble and volume. The tone control 2 feeds the compressed current frequency adjusted by the tone control to the earpiece 5 via the high gain current amplifier 4, which may have a current gain control.

9

The compressor 2, which will be described hereinafter with reference to Figures 11 and 12, comprises CMOS transistors operating in weak inversion. The compressor preferably has a sensitivity control which controls the slope (gain) of the transfer function of the compressor as shown in Figure 12.

An example of the tone control 3 is shown in Figure 8 and will be described hereinafter. The tone control is an analogue circuit comprising field effect transistors operating in weak inversion. It provides adjustment under the control of the user of the frequency response of the hearing aid and of volume.

The current amplifier 4 also comprises field effect transistors operating not in weak inversion mode, but with very small currents. The amplifier 4 amplifies the very small current (e.g. nano-amps) output by the tone control 3 to a current (e.g. micro-amps) sufficient to activate the earpiece.

The compressor 2, the tone control 3 and the amplifier 4 may be integrated into a single analogue Integrated Circuit indicated by box 6.

The hearing aid of Figure 1 has extremely low power consumption and allows the user to control at least the frequency response and volume. The hearing aid may be controlled, via an interface 7, by a wireless remote commander 8.

The audio signal processor of Figure 1 may be used for audio signal processing in applications other than hearing aids.

20 Single Channel Cochlear Implant

5

10

15

25

30

Figure 2 shows an illustrative example of a single channel Cochlear Implant according to the invention. This single channel embodiment of the invention operates entirely in the analogue domain.

A microphone 21 produces audio voltage signals which are fed to a compressor 22 which converts the voltage signals to audio current signals. The compressor circuit 22 process the signal into a certain dynamic range appropriate for the specific individual. The dynamic range of the output current is controlled by the compressor. The dynamic range that contains most of the area of speech sounds is from about 40dB to 80dB and, the dynamic range for electrical stimulation is narrow, in the region between 2dB and 20dB varying from individual to individual. In order to perform the electrical compression of the signal the compressor 22 converts voltage to

current. That is, the dynamic range of voltage is converted into the dynamic range of current. Here, dynamic range stands for the range between the threshold and uncomfortable levels of hearing. An example of a compressor is shown in Figure 11. Preferably the compressor allows the adjustment of the dynamic current range by means of a current control. In this example the VIC acts as a sensitivity as well. The amplifier/compressor 2 is implemented by an MOS circuit operating in the weak inversion mode. Because the weak inversion mode is exponential (or natural logarithmic) in characteristic, it effects compression in a manner compatible with the exponential characteristic of the Cochlear.

A tone control 32 allows the user to adjust the frequency response of the system whilst the system is in use:- that has not been possible before in a Cochlear Prosthesis. A circuit useful in the tone control will be described with reference to Figures 8 and 9. A current amplifier 24, having a current gain control, amplifies the current output by the tone control 23 and provides it to a biphase signal generator 27 which applies a biphase current to a single implantable electrode 28.

15

20

30

Referring to Figure 3, a biphase signal is a sampled signal having successive samples each comprising sub-samples S1 and S2 etc. of opposite polarity; that is a positive current pulse followed by a negative current pulse. The samples are of the audio signal produced by the tone control and the current amplifier. A biphase signal is needed to energize an electrode implanted in the Cochlea because applying only pulses of one polarity desensitizes the nerve endings. In the biphase signal generator 27, an oscillator 29 (which may be controllable) produces a "square wave" voltage 301 oscillating between a positive limit and a negative limit. The amplified output current of the tone control amplitude modulates the square wave 301 to produce the sampled biphase current signal 302. It will be appreciated that for simplicity Figure 3 is schematic and assumes modulation by a sine wave. The frequency of the biphase oscillator is preferably variable by the patient. The sampling rate may a rate known in the art. Although the sampling rate could comply with Nyquist in practice it is much lower and each sample is a burst of varying audio as shown in Figure 3 at S! and S2.

Referring to Figure 4 the signal which amplitude modulates the square wave is a full-wave rectified signal 401 which is produced by the tone control 23 so that the

Cochlear implant does not stimulate in a silent environment. Ignoring the effect of the tone control, full wave rectification is achieved by producing two audio currents 402 and 403 of opposite phase, rectifying each (e.g. by shifting the DC levels of the currents) to produce half wave rectified currents 404 and 405 and adding the currents 404 and 405 using an adder 25.

Referring to Figures 2, 4 and 5, the currents 402 and 403 of opposite phase are produced by complementary outputs of the compressor 22 and fed to the tone control 23. The tone control includes two identical circuits 3A and 3B (an example of which will be described with reference to Figure 8). The circuits 3A and 3B process the respective signals 402 and 403. Each circuit 3A and 3B comprises a pair of low pass filters 221 and 222 having different pass bands. A subtractor 223 subtracts the outputs of the two circuits to produce a band-pass filtered signal as shown in Figure 5. The half wave rectification by DC level shifting may take place in the subtractor 223.

The system of Figure 2 may comprise a housing containing the microphone 1, amplifier/compressor 22 tone control 23, the amplifier 24 and the biphase signal generator 7 and which is worn by the user. The compressor 22, the tone control 23, the amplifier 24 and the biphase signal generator 27 are preferably integrated into a single chip analogue integrated circuit 62. As will be described with reference to Figure 10, at least the tone control 23 may be controlled by a wireless remote commander.

Multi-channel Cochlear Implant

15

20

25

30

Figure 6 shows another embodiment of a Cochlear Implant according to the invention and which also operates entirely in the analogue domain. The embodiment is a multi-channel embodiment having an array of electrodes 81 to 84 which in use are implanted in the ear. In the example of Figure 6 only four channels are shown. In other examples there are at least two channels, and there may be more than four channels. A microphone 61, and compressor 62 similar to those of Figure 2, produce compressed audio current signals. The compressor 62 is arranged to produce oppositely phased signals on respective outputs. The oppositely phased signals are fed to tone control circuits 3A and 3B as will be described with reference to Figures 8 and 9. Each circuit 3A, 3B comprises two low pass filters 221, 222, the outputs of which

are fed to respective subtractors 623. Unlike the subtractor 223 of the system of Figure 2, the subtractors 623 of Figure 6 produce unrectified, oppositely phased, current signals. The pair of unrectified opposite phase current signals are fed to respective arrays of band-pass filters 101A to 104A and 101B to 104B. Band pass filters 101A and B have the same filter characteristic and produce corresponding filtered signals of opposite phase. The other band pass filters 102A to 104A and 102B to 104B likewise produce correspondingly filtered signals of opposite phase. The band pass filtered signals are fed to half wave rectifiers 11, for example DC level shifting circuits. Corresponding half wave rectified signals of opposite phase are summed in adders 91 to 94 to produce full wave rectified signals which are amplified in respective current amplifiers 41 to 44. The fullwave rectified current signals produced by the amplifiers 41 to 44 correspond to different pass bands defined by the filters 101 to 104.

5

10

15

20

25

30

A circuit comprising MOS transistors, the transistors operating in weak inversion, is preferably used to implement the Band-pass filters 101 to 104 of Figure 6. An example of a suitable circuit is described with reference to Figure 13.

The fullwave rectified current signals produced by the amplifiers 41 to 44 are fed to an interleaving circuit 12 which samples the signals and interleaves the samples to produce Continuously Interleaved Samples which are biphase modulated and applied to the array of Cochlear Implant electrodes 81 to 84. An oscillator 69 produces a biphase square voltage wave. Referring to Figures 6 and 7, there are in effect four channels (in this example) associated with respective pass bands. One channel comprises the pair of band pass filters 101A and B the adder 91 and the electrode 81. The other channels likewise comprise a pair of band pass filters(102A,B; 103A,B; and 104A,B) an adder (92, 93, 94) and an electrode (82, 83, 84). Thus each of the electrodes 81 to 84 is associated with a respective one of the pass bands. The interleaving of the samples is controlled by the interleaving circuit 12. The interleaving circuit activates each channel in turn: when one channel is active all the other channels are inactive. Referring to Figure 7, the circuit 12 sequentially connects: electrode 81 to filter 101A,B; the electrode 82 to filter 102A,B; the electrode 831 to filter 103A,B; and the electrode 841 to filter 104A,B etc.. Each

13

electrode receives a positive and a negative current pulse which together form one sample.

The system of Figure 6, except for the microphone 61, the controls and the electrodes may be integrated into a single analogue integrated circuit 65.

Various modifications may be made to the Cochlear implants of Figures 2 and 6. For instance, the pulses produced by the oscillator 29, 69 may be controlled by a control 291, 691. The pulse repetition rate and/or the pulse widths may be varied. The sampling rate for each electrode may be a rate known in the art for Continuous Interleaved Samples. Although the sampling rate could comply with Nyquist in practice it is much lower and each sample is a burst of varying audio as shown in Figure 3 at S! and S2.

The design of the illustrative Cochlear Implant prosthesis described with reference to Figures 2 and 6 focuses on two areas:

i) Low-power electronics:

5

10

20

25

30

The system focuses upon a new design of analogue electronics architecture. The core of the design, especially the tone control and the bandpass filters, makes use of CMOS transistors operating in weak inversion. Other parts of the system operate in the micro-power regime and preferably in weak inversion.

ii) 'Tone-Control' for a single channel system and for a multi-channel system:

In the multi-channel system the tone control is preferably common to all channels to provide instantaneous adjustment over all channels. The tone control is based upon two low pass filters and a current subtractor.

As will be described with reference to Figure 8, the tone control comprises CMOS transistors which operate in weak inversion (sub-threshold mode) in current mode and the circuit structure is based on the 'log-domain' for building the filters tunable in the audio frequency range.

Tone Control

Figures 8A to C together show a tone-control circuit useful in the hearing aid of Figure 1 and in the systems of Figures 2 and 6. The tone control as shown in Figure 8A comprises two first-order log-domain filters 221 and 222 and a subtractor

223 or 623 built with CMOS transistors operating in weak inversion. The tone-controller is capable of providing bass cut/boost and treble cut/boost operation as shown in Figures 9A and 9B.

5

10

- 15

20

25

30

The role of the tone controller is to boost/cut the low/high frequencies of the audio range. This is accomplished by the implementation of a flexible frequency shaping function which facilitates the selective placement of poles and zeros on the complex plane. In the embodiments of the invention shown in Figures 2 and 6, the tone-controller is a subsystem of an all-analogue implementation of Cochlear Implant device where physical constraints such as size and power consumption dictate the necessity of its implementation in an analogue very low power environment, particularly without the incorporation of conventional active (e.g. op-amps) or resistive elements. More specifically, even for a diseased Cochlea the hearing sensation depends upon the frequency of the incoming signal. For a diseased Cochlea with greater sensitivity at low frequencies than at high frequencies (or vice-versa) the tone control will act to balance the hearing sensation to a comfortable level. The design of the circuit of Figures 8 and 9 is based on the log-domain design technique [4-5] which exploits the intrinsic non-linear (exponential) behavior of a transistor and provides extended dynamic range under low power supply levels. In [6] it was shown that this technique is suited for use with MOS transistors in weak-inversion mode (or sub-threshold mode [8]) of operation. In addition to the wide dynamic range possible with the log-domain technique, the design versatility offered by the implementation provides for ease and flexibility of tuning. In addition the exponential characteristic of MOS transistors operating in weak inversion and the log-domain design matches the exponential response of the Cochlea.

For the specific application for which the tone-controller is intended, a bass-cut treble-cut operation is of primary importance as the controller operates in conjunction with a separate volume control section, for example, the amplifier/compressor 2 or the current multiplier 24, 41-44. Hence a "two pole - one zero" frequency shaping network is appropriate. This is achieved by using a pair of first-order low-pass log-domain filters 221 and 222 which are built by means of MOS transistors operating in

10

15

weak-inversion and which are tuneable in the audio frequency range. The output signal is the difference produced by a subtractor 223, 623 of the outputs of the two filters.

An example of one of the log-domain filters is shown in Figure 8B. As is known from [4], [5] and [6], the log-domain filter comprises a log-compressor 801, a filter cell 802, a DC level shift 803, and an exponential expander 804.

The log compressor 801 includes a current source 806 having an input 805 for receiving an input current Iin from the voltage to current converter 2 or 22, Iin is the compressed audio current signal. The current source 806 produces a current Iin + Ib. The filter cell 802 includes a current source 807 producing a current Id. The DC level shifter 803 has current sources 808 and 809 producing currents Io which are controllable by a control input 810.

By selection of Id and Io the filter operates as a low pass filter. By varying Io, the response of the filter is varied as shown in Figure 9A or 9B.

As shown in Figure 8C, two filters 221, 222 (each as shown in Figure 8A) including the current sources are implement entirely in MOS transistors operating in weak inversion. Filter 222 is coupled to the subtractor by a high impedance buffer 888. The output current lout (s) of the subtractor 223, 623 is given by lout(t) =

$$\frac{I_{02} \cdot I_{b2}}{I_{d2}} - \frac{I_{01} I_{b1}}{I_{d1}} + L^{-1} \left[\frac{I_{02}}{I_{d2}} - \frac{I_{01}}{I_{d1}} \right] \frac{1 + \frac{s}{I_{d2} (c_1 \cdot nV_t)} - \frac{I_{01} (c_2 \cdot nV_t)}{I_{d1} \cdot I_{d2}}}{1 + \frac{s}{I_{d2}} - \frac{I_{d1}}{I_{d1}}} I_{in,ac}(s)$$

Equation 1

In Equation 1, Vt is the thermal voltage kt/q of the MOS transistors, n is a process parameter and L¹ is the inverse Laplace transform. The meaning of the other terms is evident from Figure 8C.

Equation 1 results in a broad passband frequency shaping network , suitable for the particular application. In the case when a tone-controller of the Baxandall type approximated by a "two-pole two-zero" function is needed, it can be implemented by feeding the input signal to the output of a log-domain lowpass 'biquad' and taking the difference as the output signal. A 'biquad' is a filter described by a biquadratic equation. The subtractor comprises transistors M2=M3=M4=M5 with W=2.4um and L=2.0 um, and transistor M1 with W=10 um and L=2.0 um, for the appropriate dc output level to be realised.

The operation of the proposed circuit was simulated with SPECTRE models and AMS 2.0 um process parameters. Figures 9A and B show the effect of the tone control at low and high frequencies. The input current is of class-A having the formula Iin(t)=Ibias,[1+m sin(wt)], m being the modulation index. When Ibias=10nA and the corner frequencies of the network is about 100 Hz and 12000 Hz, an input tone of 1000 Hz modulated by m =20, 30 and 40 % exhibits a THD level of -58.2 dB, -55 dB and -56.2 dB respectively. For the same corner frequencies two equal amplitude sinusoidal tones with frequencies equal to 900 Hz and 1100 Hz and modulated by m = 40 % exhibited an InterModulation Distortion (IMD) level of -46.3 dB. (IMD is distortion produced when two signals are simultaneously applied to the filter.)

15

20

25

30

Thus a specific tone controller suitable for a micropower environment has been described by way of example. The circuit comprises two log-domain lossy integrators 221 and 222 and a subtractor 223 and takes advantage of the exponential behaviour of the MOS transistors when operated in weak inversion to match the characteristics of the Cochlea. The good dynamic range offered by the log compression coupled with flexible tuning adaptability are highly advantageous when attempting to realise an implantable analogue silicon device as a biological auditory prosthesis. The System described herein-above mainly focuses upon a new design of electronics architecture, resulting in smaller size and lower power consumption. The design is able to be applied to a multichannel CIS strategy and it also has the capability to provide a complex pulsatile stimulus to a short, single-channel electrode.

Referring to Figure 10, the integrated circuit block 62 or 65 represents the parts of the embodiments of Figures 2 and 6 which are integratable into a single analogue chip. The chip has control inputs S,B,T,V, and O for sensitivity, bass, treble, volume and oscillator control. A control interface 120 provides control signals to operate the controls S,B,T,V, and O. The interface receives signals transmitted to it wirelessly from a remote commander 121.

Voltage to Current Converter

Figure 11 is a simplified circuit diagram of an example of the voltage to current converter 2, 22, 62 which compresses the dynamic range of the audio signal. The converter is an operational transconductance amplifier having an NMOS differential pair gain stage as known in the art. The converter has oppositely phased outputs Ido_1 Ido_2 at which currents proportional to the currents Id_1 and Id_2 are produced as required by the system of Figure 6. If the converter is used in the system of Figure 2, only one of the outputs is used. The converter has a current source 111. The current Ic through the current source 111 is varied to control the gain of the converter, and thus the sensitivity, as shown in Figure 12.

The NMOS transistors are operating in weak inversion.

20

5

10

15

$$I_{d1} = \frac{I_c.e^{+x}}{1 + e^{+x}}$$

$$I_{d2} = \frac{I_c.e^{-x}}{1 + e^{-x}}$$

$$x = \frac{V_1 - V_2}{n.V_i}$$

where n is a process parameter and Vt = kT/q.

 Id_1 and Id_2 are non-linear with a quasi-linear region. The non-linearity approximately matches the characteristics of the ear. The non-linearity outside the quasi-linear region compresses large current amplitudes to prevent over-stimulation of the Cochlear.

Band Pass Filter

5

10

20

25

Figures 13A to 13D are diagrams illustrating the construction and operation of one of the band-pass filters 101 of the system of Figure 6. The band-pass filter is based on the work of Frey as described in [4], but is novel in itself.

As shown in Figures 13A and 13B, basic units of the filter are an E+ cell and an E- cell. An E+ cell operates with the positive power supply and an E- cell operates with the negative power supply. Each cell is implemented in CMOS.

For both E+ and E- cells, the output current Iout(t) is related to the input current Iin(t) by

$$I_{OUT}(t) = \left(\frac{W}{L}\right)_{M_3, M_4} \left(\frac{L}{W}\right)_{M_3, M_3} \cdot i_{in} \frac{V^+ - V^-}{e^{2\pi V_i}}$$

where M1, M2, M3, M4 are the transistors indicated in Figures 13A and 13B, W is the channel width, L is the channel length, and Vt is the thermal voltage kT/q.

The E+ and E- cells are combined as shown in Figure 13C to form a log-domain band-pass filter. The filter is shown in more details in Figure 13D. In Figures 13C and 13D:-

In is the input current,

Iout is the output current,

Idc₁ and Idc₂ are bias currents,

Io is a current defining the tuning frequency of the filter,

n is a process parameter range between 1 and 1.5, and

Q is the quality factor of the filter.

The transfer function of the filter is

20

25

30

$$H(s) = \frac{I_{out}(s)}{I_{in}(s)} = \frac{\left(\frac{I_d}{C.n.V_i}\right)s}{s^2 + \left(\frac{I_d}{C.n.V_i}\right)s + \left(\frac{I_0}{C.n.V_i}\right)^2}$$

where Vt is the thermal voltage kT/q, and n is the process parameter.

The tuning frequency wo of the filter is

$$\omega_0 = I_0/C.n.V_{t_i}, \quad Q = I_0/I_d, \quad I_d = I_0/Q$$

10 $V_{02} = 2.n. V_t ln[I_{dc2}/I_{dc1}], I_{dc2} = I_0[1 + 1/Q], V_0 = 2.n. V_t ln[(I_{in} + I_{dc1})/I_{d0}]$ where Ido is the saturation current.

Alternative Multi-channel Cochlear Implant

Figure 14 shows another embodiment of a Cochlear Implant according to the invention and which also operates entirely in the analogue domain. The embodiment is a multi-channel embodiment having an array of electrodes 81 to 84 which in use are implanted in the ear. In the example of Figure 14 only four channels are shown. In other examples there are at least two channels, and there may be more than four channels. A microphone 61, and compressor 62 similar to those of Figure 2, produce compressed audio current signals. The compressor 62 is arranged to produce oppositely phased signals on respective outputs. The pair of unrectified opposite phase current signals are fed to respective arrays of band-pass filters 101A to 104A and 101B to 104B. Band pass filters 101A and B have the same filter characteristic and produce corresponding filtered signals of opposite phase. The other band pass filters 102A to 104A and 102B to 104B likewise produce correspondingly filtered signals of opposite phase. The band pass filtered signals are fed to half wave rectifiers 11, for example DC level shifting circuits. Corresponding half wave rectified signals of opposite phase are summed in adders 91 to 94 to produce full wave rectified signals which are amplified in respective current amplifiers 41 to 44. The fullwave rectified current signals produced by the amplifiers 41 to 44 correspond to different pass bands defined by the filters 101 to 104.

A circuit comprising MOS transistors, the transistors operating in weak inversion, is preferably used to implement the Band-pass filters 101 to 104 of Figure 14. An example of a suitable circuit is described with reference to Figure 13.

5

10

15

20

25

30

The fullwave rectified current signals produced by the amplifiers 41 to 44 are fed to an interleaving circuit 12 which samples the signals and interleaves the samples to produce Continuously Interleaved Samples which are biphase modulated and applied to the array of Cochlear Implant electrodes 81 to 84. An oscillator 69 produces a biphase square voltage wave. Referring to Figures 6 and 7, there are in effect four channels (in this example) associated with respective pass bands. One channel comprises the pair of band pass filters 101A and B the adder 91 and the The other channels likewise comprise a pair of band pass filters(102A,B; 103A,B; and 104A,B) an adder (92, 93, 94) and an electrode (82, 83, 84). Thus each of the electrodes 81 to 84 is associated with a respective one of the pass bands. The interleaving of the samples is controlled by the interleaving circuit 12. The interleaving circuit activates each channel in turn: when one channel is active all the other channels are inactive. Referring to Figure 7, the circuit 12 sequentially connects: electrode 81 to filter 101A,B; the electrode 82 to filter 102A,B; the electrode 831 to filter 103A,B; and the electrode 841 to filter 104A,B etc.. Each electrode receives a positive and a negative current pulse which together form one sample.

In accordance with this embodiment of the invention, a tone generator 141 is connected to the input of the compressor 62. The tone generator 141 and the current amplifiers 41 to 44 are controlled by a remote control system comprising a remote commander 143 operable by the patient and a remote control interface 142 which respond to control signals transmitted to it from the commander 143 to control the tone generator 141 and the amplifiers 41 to 44.

The tone generator is arranged to selectively generate respective tones at the fundamental frequencies of the filters 101 to 104. The tone which is generated is selected by the remote control system. The remote control system allows the volume of each channel of the Cochlear Prosthesis to be adjusted by controlling the gain of the current multipliers. The remote control 143 has channel selection buttons CH1 to

CH4, a store button and one (or in this example two) volume control buttons. In this example there is one button for increasing volume and another for reducing volume. The patient selects one e.g. CH1 of the channels using one of the channel selection buttons. Selecting one channel CH1 mutes all the other channels CH2 to 4 by reducing the gains of the amplifiers 42 to 44 of the other channels to zero. Selecting one channel CH1 also causes the tone generator to generate a tone of preset amplitude having the fundamental frequency of the filter 101 of that channel. The patient then adjusts the gain of the amplifier 41 of the selected channel CH1 to a preferred value between the threshold and uncomfortable levels of hearing using the volume control buttons on the remote control. The interface 142 stores the selected value for example in response to actuation of the store button so that the setting is not lost when another channel is adjusted. Thus the patient has control of the programming of volume of the 'MAP'. The patient is preferably guided through the adjustment process by a skilled technician.

The fundamental frequencies of the filters are fixed in this example. The fixing of the fundamental frequencies may be done by a skilled technician when the prosthesis is first fitted to the patient. In other embodiments of the invention the filter frequencies may be adjusted by the user using the remote control system but such adjustment is currently considered to be too difficult for an unskilled user.

References

5

- [1] I.R.Sinclair, "Audio Electronics Reference Book", pp. 373-383 BSP Professional Books, 1989
- [2] R. F. Graf & W. Sheets, "Encyclopaedia of Electronics Circuits", Vol. 6, pp.653, Mc-Graw Hill 1996
- [3] J.Markus, "Modem Electronics Circuits Reference Manuals", pp.61, McGraw
 Hill 1980
 - [4] D.R.Frey, "Log-domain filtering: an approach to current-mode filtering", IEE Proceedings-G, vol. 140, pp. 406-416, 1993.
- 15 [5] D.R.Frey, "Exponential State-Space Filters: A generic current-mode design strategy", IEEE CAS -1, Vol. 43, No. 1, pp. 34-42, 1996
 - [6] C.Toumazou, J. Ngarnmil and T.S. Lande, "Micropower log-domain filter for electronic cochlea", Electronics Letters, Vol. 30, No. 22, pp. 1839-1841, 1994.
 - [7] W.F. House, Cochlear Implants: "My Perspective"- Cochlear Implant Monographs.
 - [8] Horowitz and Hill, The Art of Electronics 2nd Edition page 122
 - [9] J. Ngarnmil C. Tournazou, and T.S. Lande, "A fully tuneable micropower log-domain filter", 21st European solid State Circuits Conference ESSCIRC'95 France. September 1995.

25

CLAIMS

- 1. An analogue signal processor, the analogue processor having an input for receiving an audio current signal, an output for delivering a processed audio signal to an audio output transducer, and log-domain filter means comprising MOS transistors operating in weak inversion for processing the audio signal.
- 2. A processor according to claim 1, wherein the said filter means is a tone control comprising first and second log-domain filters having different low-pass bands and a subtractor for subtracting the output currents of the filters to produce a band-pass filter characteristic.
- 3. A processor according to claim 1 or claim 2, further comprising a compressor coupled to the said input for compressing the dynamic range of the audio signal.
 - 4. A processor according to claim 3, wherein the compressor is a voltage to current converter.
- 5. A processor according to claim 3 or 4, wherein the compressor comprises MOS transistors operating in weak inversion.
 - 6. A processor according to claim 5, wherein the compressor provides control of sensitivity.
 - 7. A processor according to claim 1, 2, 3, 4 5 or 6, further comprising an amplifier coupling the filter means to the output.
- 8. A processor according to any one of claims 1 to 7 implemented as a single chip analogue MOS integrated circuit.

24

- 9. A processor according to anyone of claims 1 to 8, wherein the audio signal is a current signal.
- 10. A hearing aid comprising a processor according to any preceding claim.

11. An analogue audio signal processor use in a cochlear implant, the processor comprising:

an input for receiving an audio signal,

5

10

15

20

an output for delivering a processed audio signal to a cochlear implant electrode and a tone control circuit for adjusting the frequency amplitude of the audio signal comprising first and second filters having different low-pass bands and a subtractor for subtracting the output currents of the filters to produce a band-pass filter characteristic,

each of the first and second filters being log-domain filters comprising MOS transistors operating in weak inversion.

- 12. A processor according to claim 11, further comprising a compressor coupling the said input to the tone control circuit, the compressor compressing the dynamic range of the audio signal.
- 13. A processor according to claim 11, wherein the compressor is a voltage to current converter.
- 14. A processor according to claim 13, further comprising a current amplifier for amplifying the output signal of the tone control circuit.
 - 15. A processor according to claim 12, 13 or 14, wherein the compressor comprises MOS transistors operating in weak inversion.
- 30 16. A processor decodes to claim 12, 13 14 or 15, wherein the compressor provides control of sensitivity.

- 17. A processor according to any one of claims 11 to 16, further comprising a biphase signal generator for delivering to the said output a biphase signal modulated by the processed audio signal.
- 18. A processor according to claim 17 further comprising means for full-wave current rectifying the processed audio signal for applying a full wave rectified audio signal as a modulating signal to the biphase generator.

15

20

25

- 19. A processor according to any one of claims 11 to 18 comprising only one output for connection to a single cochlear implant electrode.
- 20. A processor according to claim 18, wherein the full-wave rectifying means comprises means connected to said input for producing, oppositely phased audio signals,

one of the oppositely phased audio signals being supplied to the said first and second filters,

third and fourth filters to which the other of the oppositely phased audio signals is supplied, having low pass bands substantially identical to the said first and second filters respectively, a further subtractor for subtracting the outputs of the third and fourth filters to produce a band-pass characteristic,

means for applying a DC offset to the filtered audio signals to effect half-wave rectification, and

- a combine for combining the half-wave rectified outputs of the subtractors to effect full-wave rectification.
- 21. A Cochlear implant prosthesis comprising a signal processor according to any one of claims 11 to 20.

22. An analogue audio signal processor for use in a cochlear implant prosthesis, comprising

an input for receiving an audio signal,

15

25.

- a plurality of outputs for connection to respective cochlear implant electrodes for delivering processed audio signal thereto, and
 - a tone control common to all the outputs for simultaneously adjusting the intensity/frequency content of the processed audio signals fed to the said outputs,

the tone control comprising MOS transistors operating in weak inversion.

- 10 23. A processor according to claim 22, wherein the said intensity/frequency content is controllable by the user of the prosthesis.
 - 24. A processor according to claim 22 or 23, wherein the tone control comprises log-domain filter means
 - 25. A processor according to claim 22,23 or 24, further comprising a compressor coupled to the said input, the compressor compressing the dynamic range of the audio signal.
- 26. A processor according to claim 25, wherein the compressor is a voltage to current converter.
 - 27. A processor according to claim 25 or 26, wherein the compressor comprises MOS transistors operating in weak inversion.
 - 28. A processor decodes to claim 25, 26 or 27, wherein the compressor provides control of sensitivity.
- A processor according to any one of claims 22 to 28, further comprising means
 for separating the intensity/frequency adjusted audio signal into a plurality of frequency separated audio signals having different frequency bands.

15

20

30

- 30. A processor according to claim 29 further comprising a plurality of biphase signal generators for supplying bi-phase signal modulated by the respective frequency separated signals to respective ones of the said outputs.
- 31. A processor according to claim 29 or 30, wherein the separating means comprises a plurality of band-pass filters.
- 32. A processor according to claim 31, wherein each band-pass filter is a logdomain filter comprising MOS transistors operating in weak inversion.
 - a processor according to claim 30, 31 or 32, comprising sampling means for applying samples of the frequency separated audio signals to the respective biphase signal generators.

34. A processor according to claim 33 wherein the sampling means comprises a continuous interleaved sample generator.

- 35. A processor according to claim 30, 31, 32 33 or 34 wherein the frequency processed audio signals are full-wave rectified.
 - 36. A Cochlear implant prosthesis comprising a signal processor according to any one of claims 22 to 35.
- 25 37. A current-mode analogue tone control circuit for use in an audio signal processor, the tone control comprising MOS transistors operating in weak inversion.
 - 38. A circuit according to claim 37 which comprising an input for receiving an audio signal, first and second filters coupled to the input and having different low-pass bands, and a subtractor for subtracting the output currents of the first and second filters to produce a band-pass filter characteristic.

- 39. A circuit according to claim 38 wherein the tone control comprises third and fourth filters, the third and fourth filter having the same low-pass bands as the first and second filters respectively,
- the third and fourth filters having an input for receiving an audio signal oppositely phased to the audio signal applied to the first and second filters, and
 - a further subtractor for subtracting the output currents of the third and fourth filters to produce band-pass filter characteristic.
- 40. A circuit according to claim 39, comprising half-wave rectifying means whereby the outputs of the subtractors are half-wave rectified and combiner for combining the half-wave rectified outputs to produce a full-wave rectified audio signal.
- 15 41. A circuit according to claim 38, 39 or 40 wherein each filter is a log-domain filter comprising MOS transistors operates in weak inversion.
- 42. A circuit according to any one of claims 37 to 41, comprising means controllable by the user of the prosthesis for adjusting the frequency response of the tone control.
 - 43. A circuit according to claim 42 comprising user controls for controlling bass cut/boost and treble cut/boost.
- 25 44. A circuit according to claim 42 or 43 comprising a user-control for controlling signal amplitude.
 - 45. A circuit according to claim 44 when indirectly dependent on claim 38, 39 or 40, wherein the or each subtractor has the control input for controlling signal amplitude.

- 46. An aural prosthetic device comprising a tone control circuit according to any one of claims 37 to 45.
- 47. A single channel analogue audio signal processor for use in a Cochlear prosthesis, and including a tone control comprising a log-domain filter having MOS transistors operating in weak inversion, and means controllable by the user of the prosthesis for adjusting the frequency response of the tone control.
- 48. A multi-channel audio signal processor for use in a Cochlear prosthesis and including a tone control common to all the channels at least the frequency response of which is controllable by the user.
 - 49. An audio signal processor for use in a Cochlear prosthesis and comprising a single channel processor according to claim 47, and means for generating from the output of the single channel processor a plurality of signals at respective ones of a plurality of outputs to provide a multi-channel processor and means for selecting single or multi-channel operation.
- 50. An analogue multi-channel audio signal processor for use with a Cochlear Prosthesis and comprising
 - an input for receiving an audio signal,

15

25

- a plurality of outputs for connection to respective Cochlear Implant electrodes,
- a plurality of analogue, signal processing channels coupled to the said input and each comprising a log-domain filter having MOS transistors operating in weak inversion, the channels being coupled to respective ones of the outputs, the intensity/frequency response of each channel being adjustable, and
- means for adjusting the intensity/frequency response of each channel.

- 51. A processor according to claim 50 wherein each channel comprises an amplifier having controllable gain and the adjusting means adjusts the gain of the amplifier.
- 52. A processor according to claim 50 or 51, wherein the adjusting means comprises means for adjusting the gain of each channel in response to control signals transmitted to the adjusting means by a wireless remote commander.
- 53. A processor according to claim 50, 51 or 52, further comprising a tone generator for generating tones of preset amplitude and of respective frequencies dependent on the fundamental frequencies of the filters.
 - 54. A processor according to claim 52, wherein the frequency of the tone produced by the generator is selected by generator control means.

- 55. A processor according to claim 54, wherein the generator control means comprises a wireless remote control means.
- A processor according to any one of claims 50 to 55 wherein each channel is adjustable independently of all the other channels.
 - A processor according to any one of claims 50 to 56, wherein the channels are coupled to the outputs via sampling means.
- 25 58. A processor according to claim 57 wherein the sampling means is a continuous interleaved sample generator.
- 59. A processor according to any one of claims 50 to 58, comprising biphase signal generators for supplying to the said outputs biphase signals
 30 modulated by the output signals of the channels.

31

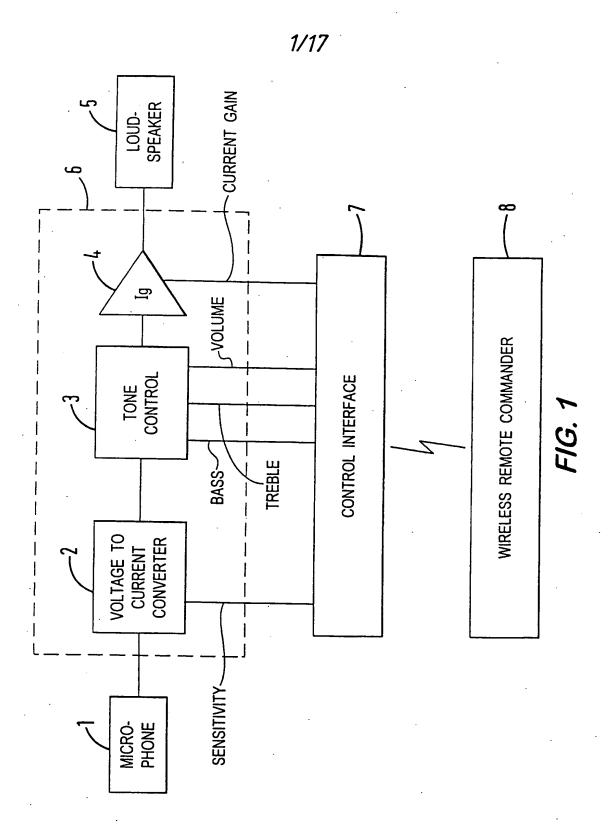
- 60. An audio signal processor and substantially as hereinbefore described with reference to the accompanying drawings.
- 61. A tone control substantially as hereinbefore described with reference to Figures 8A and 8B optionally together with Figures 9A and 9B of the accompanying drawings.
 - 62. A single-channel signal processor for a Cochlear implant prosthesis and substantially as hereinbefore described with reference to Figure 2 optionally together with one or more of Figures 8 and 11.
 - 63. A signal processor for a multi-channel Cochlear implant prosthesis and substantially as hereinbefore described with reference to Figure 6 optionally together with one or more of Figures 8, 11 and 13.

15

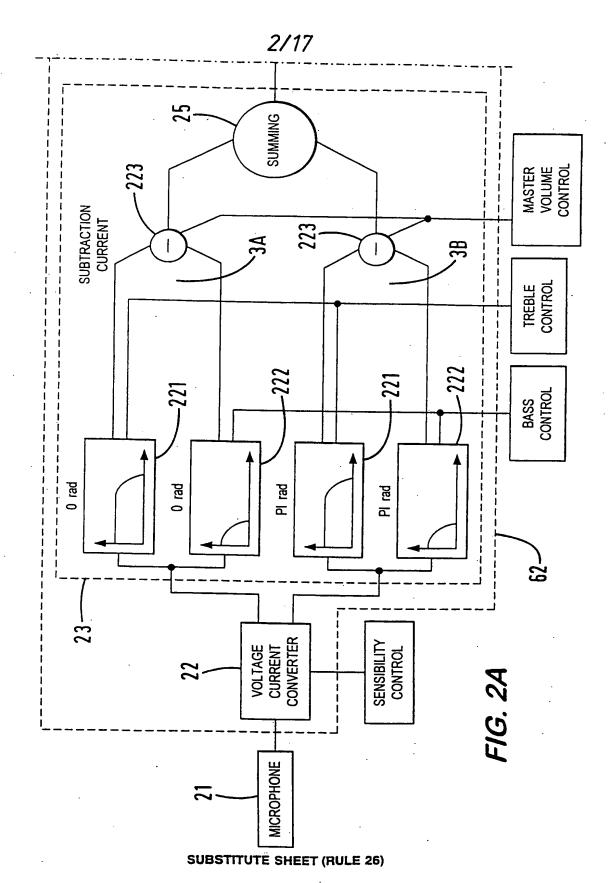
10

- 64. An audio signal processor for a hearing aid and substantially as hereinbefore described with reference to Figure 1 optionally together with one or more of Figures 8 and 11.
- 20 65. A signal processor for a multi-channel Cochlear implant prosthesis and substantially as hereinbefore described with reference to Figure 14 optionally together with one or more of Figures 11 and 13.

PCT/GB99/00055

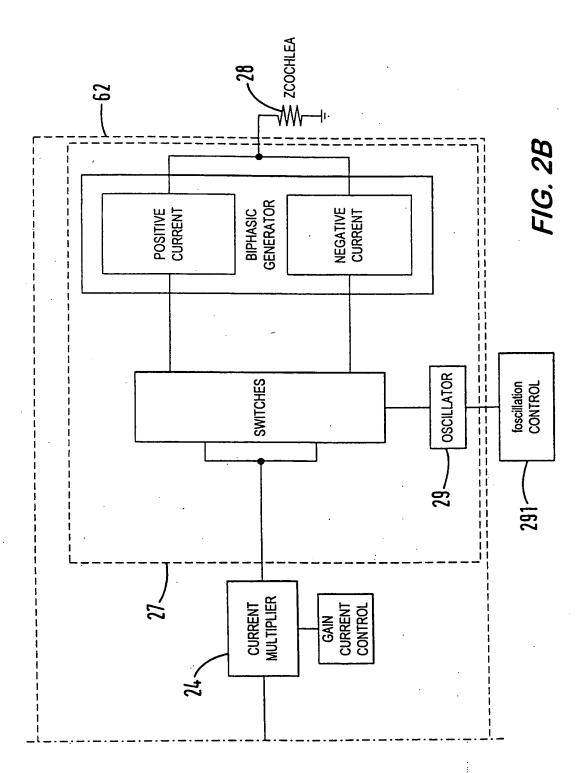


SUBSTITUTE SHEET (RULE 26)

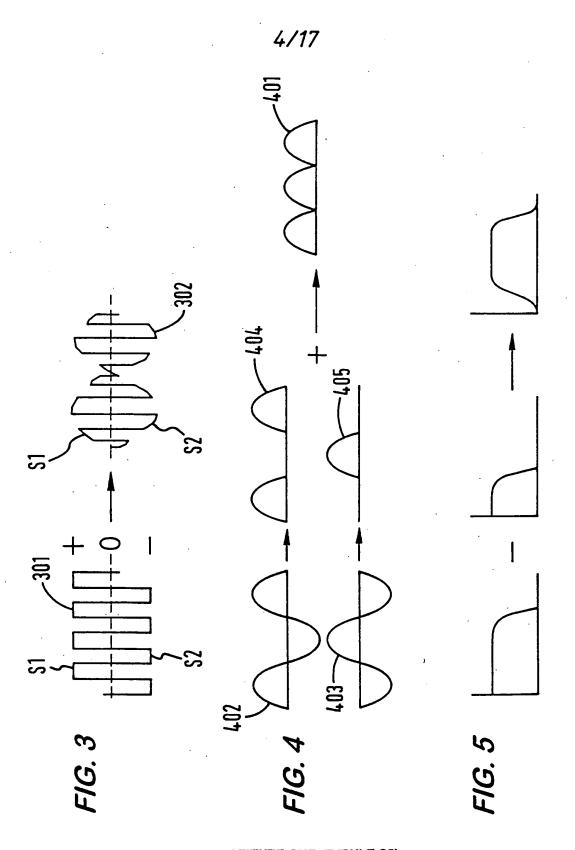


PCT/GB99/00055

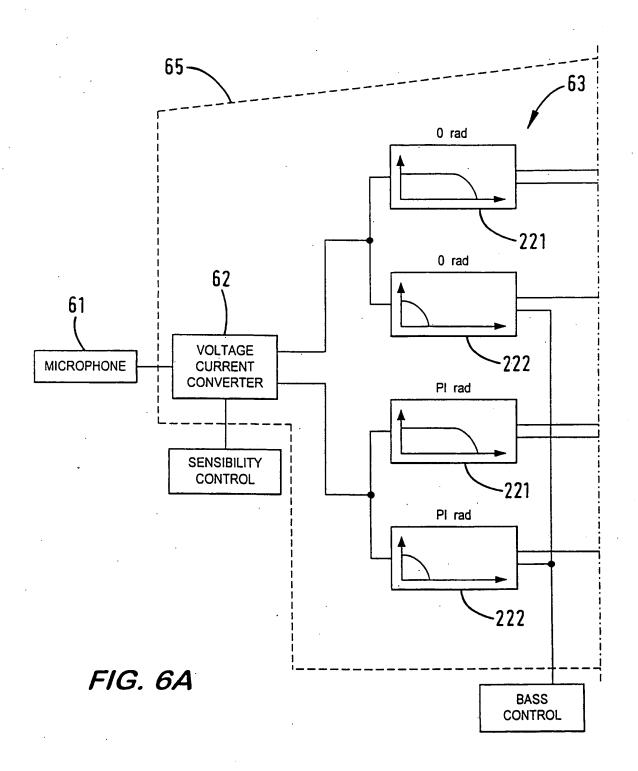




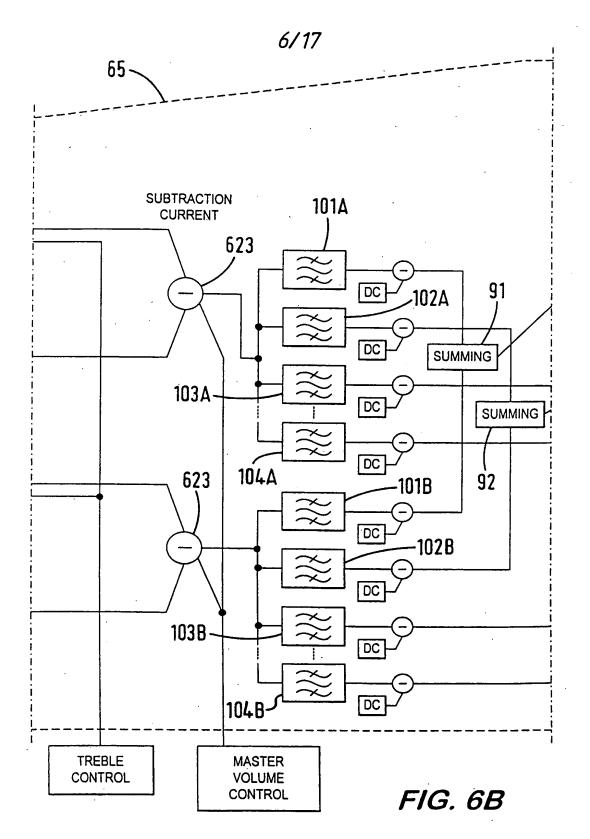
SUBSTITUTE SHEET (RULE 26)



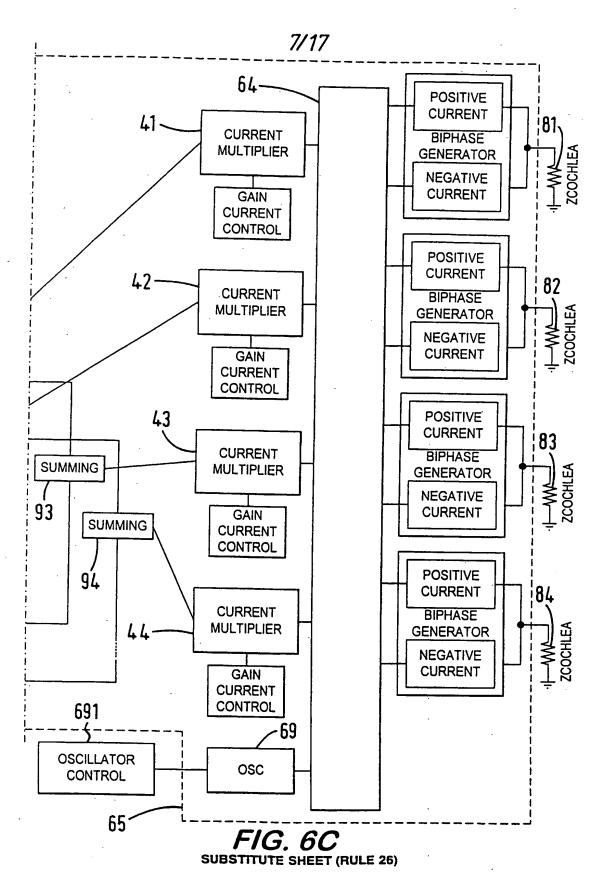
SUBSTITUTE SHEET (RULE 26)



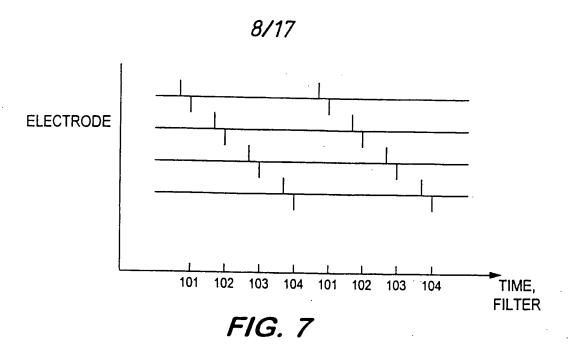
PCT/GB99/00055

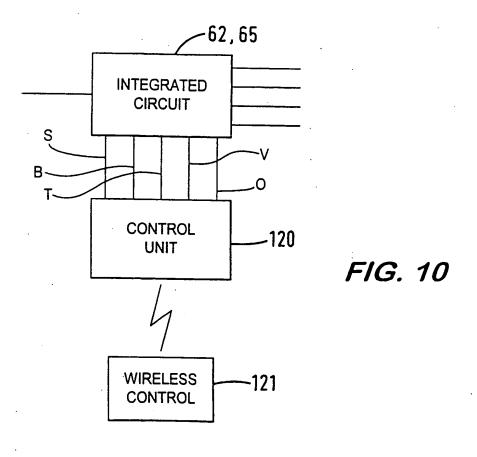


SUBSTITUTE SHEET (RULE 26)

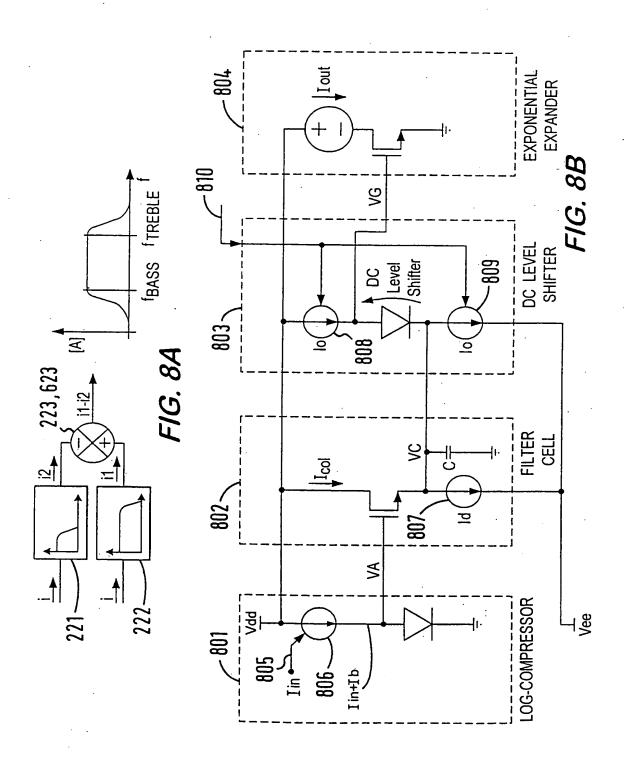


PCT/GB99/00055





SUBSTITUTE SHEET (RULE 26)

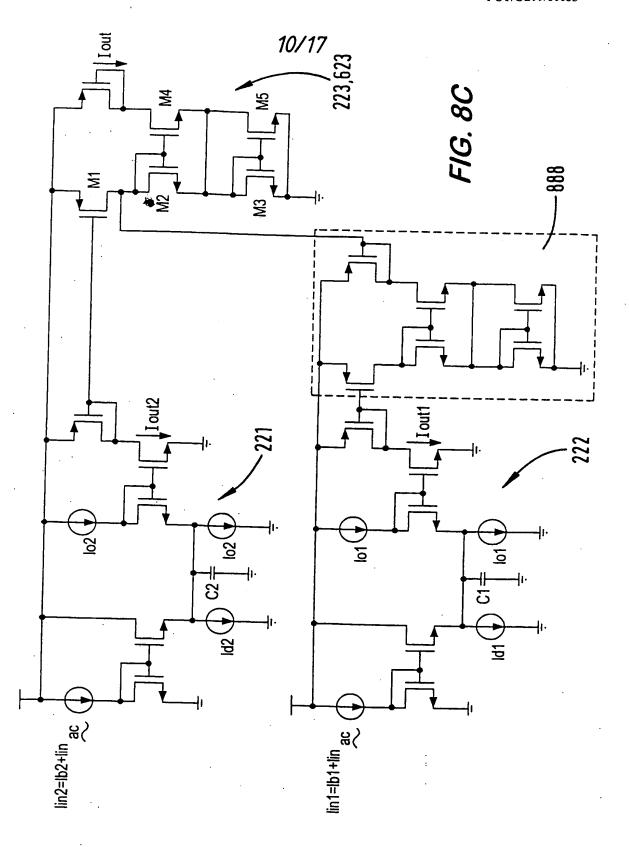


SUBSTITUTE SHEET (RULE 26)

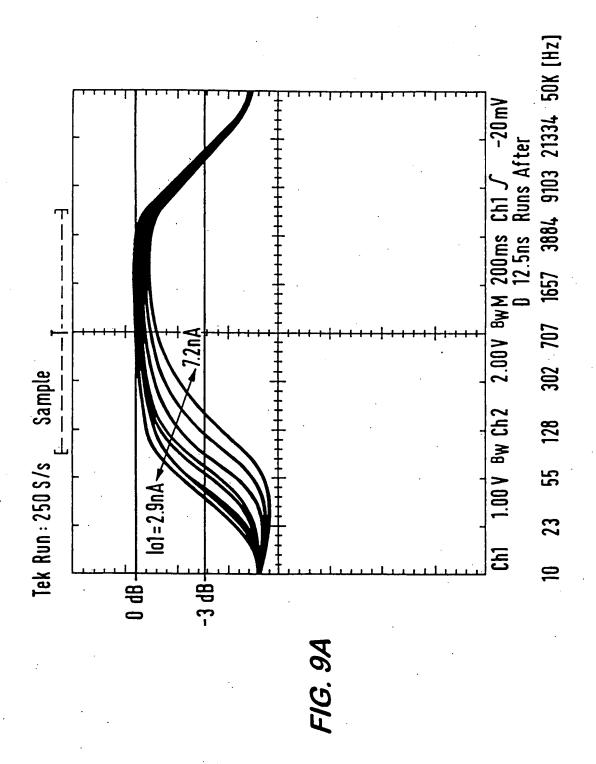


WO 99/35882

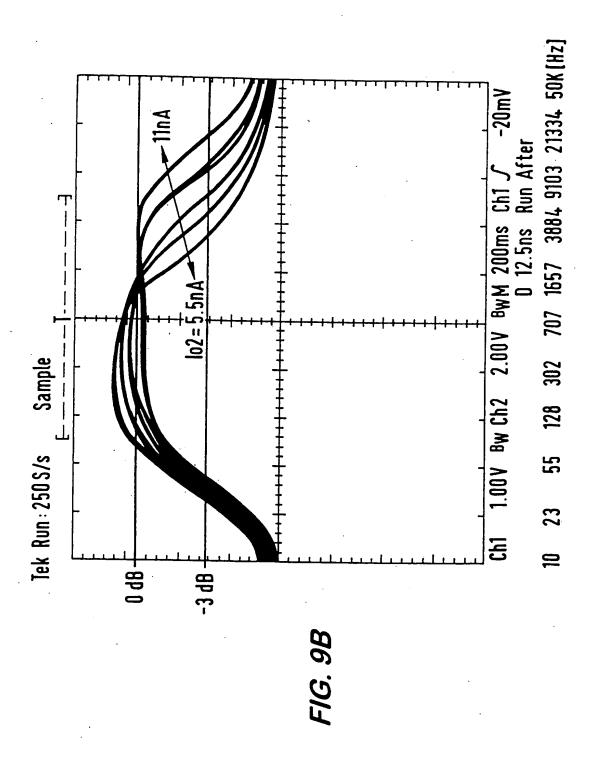
PCT/GB99/00055



SUBSTITUTE SHEET (RULE 26)

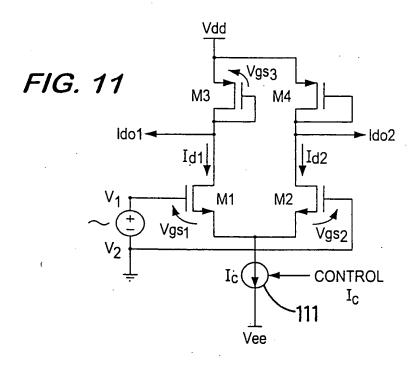


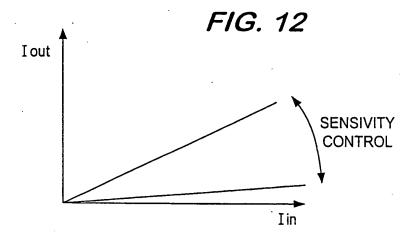
SUBSTITUTE SHEET (RULE 26)



SUBSTITUTE SHEET (RULE 26)

PCT/GB99/00055





PCT/GB99/00055

14/17

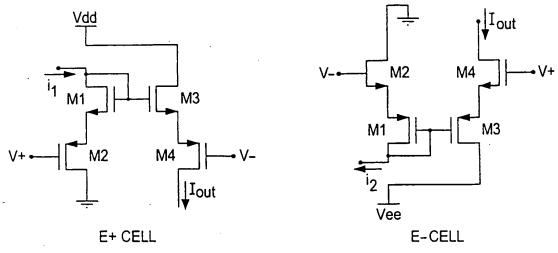


FIG. 13A

FIG. 13B

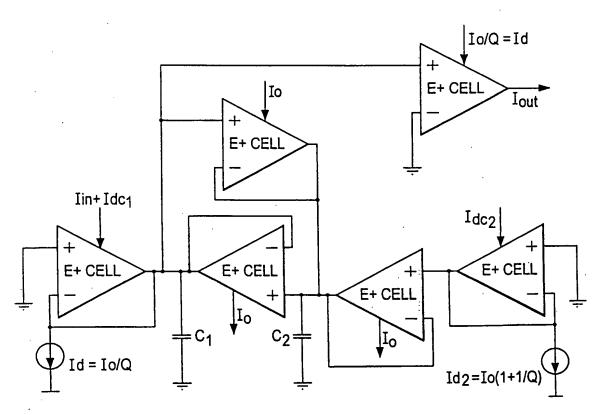
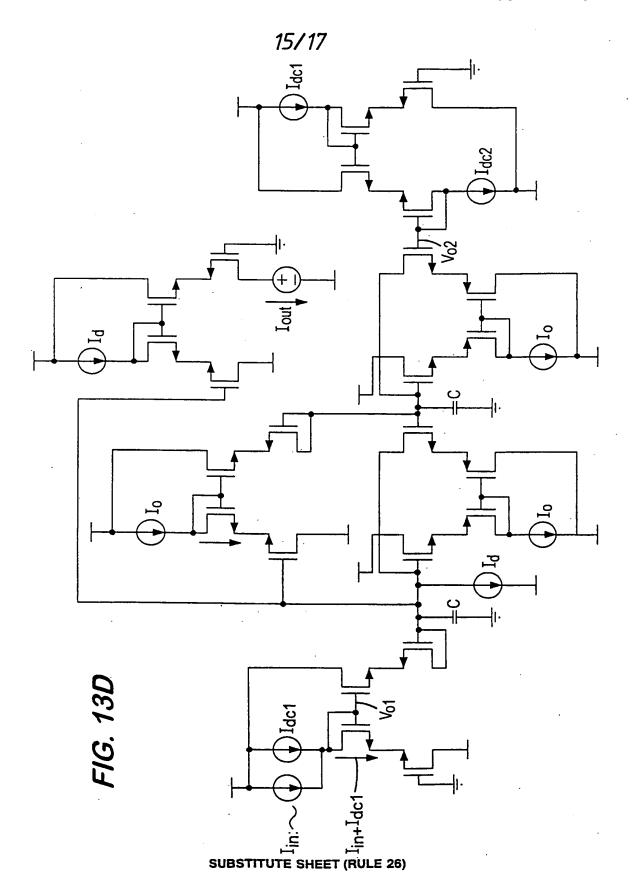


FIG. 13C

SUBSTITUTE SHEET (RULE 26)



WO 99/35882

PCT/GB99/00055

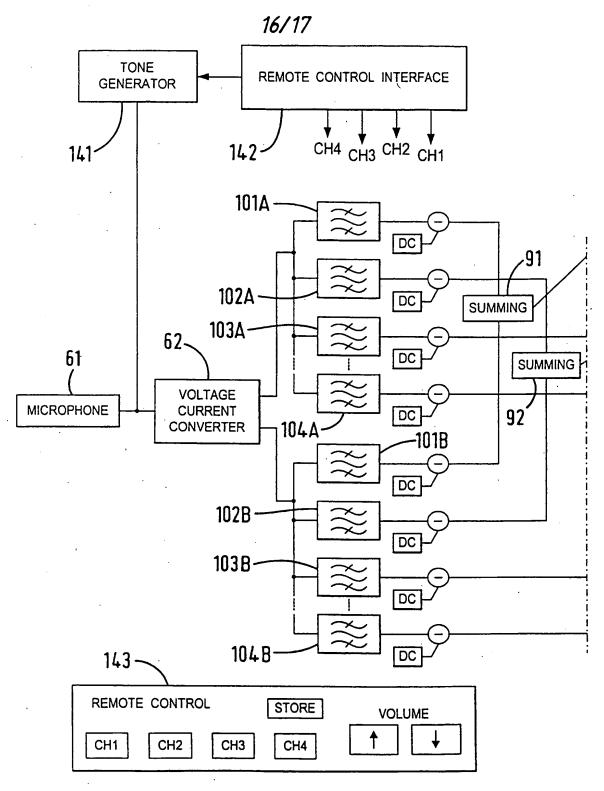
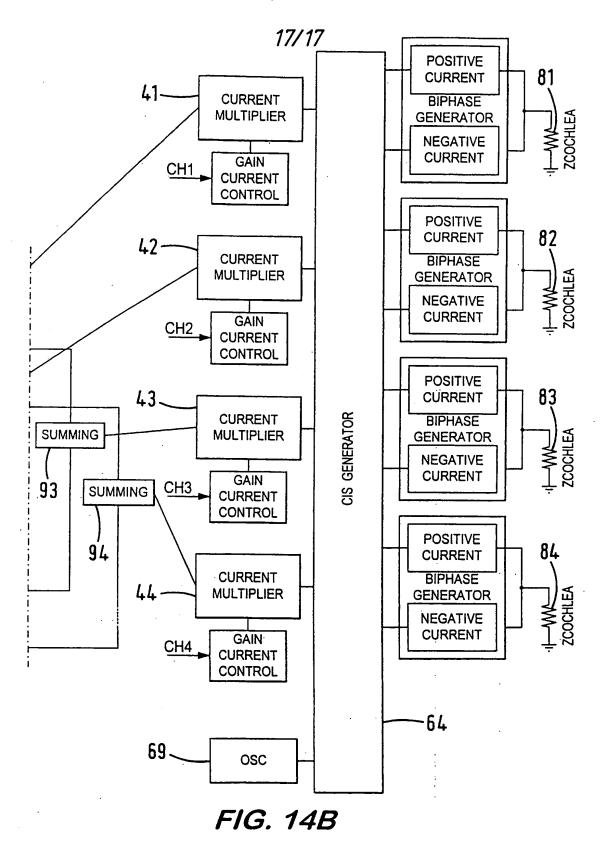


FIG. 14A

SUBSTITUTE SHEET (RULE 26)



SUBSTITUTE SHEET (RULE 26)

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

A 1' At -		- N - Cl f					
Applicant's or agent's file reference P003839WO RWP FOR FURTHER				CTION		ation of Transmittal of Interior Examination Report (Form	
Internationa	i appli	cation No.	International filing date (d	day/month	/year)	Priority date (day/month/	year)
PCT/GB99/00055 08/01/1999						12/01/1998	
Internationa H04R25/0		nt Classification (IPC) or na	tional classification and IPC	C	-		
Applicant					-		
IMPERIA	L CC	LLEGE OF SCIENCE	TECHNOLOGYe	et al.		····	
		tional preliminary exami mitted to the applicant a		prepared	by this Inte	ernational Preliminary Ex	camining Authority
2. This P	REPO	RT consists of a total of	7 sheets, including this	s cover st	neet.		
be (s	een a see Ri	port is also accompanied mended and are the bas ule 70.16 and Section 60 exes consist of a total of	sis for this report and/or 07 of the Administrative	sheets c	ontaining re	ctifications made before	
mese	anne	·	o sneets.				
3. This re	eport	contains indications rela	iting to the following iten	ns:			
	Ø	Basis of the report					
11		Priority				12 1 42 6	tta.
III			·	veity, inv	entive step	and industrial applicabil	ilty .
			nder Article 35(2) with re		novelty, inve	entive step or industrial	applicability;
			• •		٠		
							•
VIII	_	Certain observations or	• •	cation			
Data of sub	missis	n of the demand		Data of	completion of	this report	
Date of Sub	11115510	in of the demand		Date or	completion of	uis report	
26/07/19	99			07.04.20	000		
		g address of the international ning authority:	al .	Authoriz	ed officer		STATE OF STA
	Euro D-80	pean Patent Office 1298 Munich +49 89 2399 - 0 Tx; 523656	6 epmu d	Nieuw	enhuis, P		(San San San San San San San San San San
		+49 89 2399 - 4465		Telepho	ne No. +49 8	9 2399 8968	Chara- Engl



International application No. PCT/GB99/00055

I. Basis of the report

1. This report has been drawn on the basis of (substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

	the	report since they	do not contain am	endments.):					,
	Des	scription, pages:	· .						
	1-2	2	as originally filed	i					
	Cla	ims, No.:	·						
	1-3	9 · .	with telefax of		21/03/2000				,
,	Dra	wings, sheets:			•				
	1/1:	2-12/12	as originally filed	Ė					
2.	The	amendments hav	ve resulted in the c	ancellation (of:		-		
		the description,	pages:			• "			
	\boxtimes	the claims,	Nos.:	40-65					
		the drawings,	sheets:						
3.	⊠		peen established as beyond the disclo				en made, sir	ice theý h	ave been
		see separate sh	neet						
4.	Add	ditional observation	ns, if necessary:						



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/00055

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes:

Claims 1-39

No: Claims

Inventive step (IS)

Yes:

Claims 10-12

No:

Claims 1-9,13-39

Industrial applicability (IA)

Yes:

Claims 1-39

No: Claims

2. Citations and explanations

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Re Item I

Basis of the report

- 1. No basis in the originally filed application could be found for:
 - -) Claim 9 when referring to claims 1-7.
 - -) Claim 21. According to the originally filed application the intensity/frequency response of the tone circuit is controllable by a user.
 - -) Claim 28 when referring to claims 14-20 (i.e. comprising a plurality of outputs).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1. Reference is made to the following documents:
 - D1: Toumazou C, Ngarnmil J and Lande T.S.: "Micropower log-domain filter for electronic cochlea", ELECTRONIC LETTERS, Vol.30, No.22, pp.1839-1841, October 1994 (Cited in the application); XP000479753
 - D2: WO-A-97 15 114 (MITEL SEMICONDUCTOR, INC. US) 24 April 1997
 - D3: US-A-4 400 590 (MICHELSON) 23 August 1983
 - D4: Hochmair-Desoyer I: "Entwicklungsstand von auf elektrischer Stimulation beruhenden Innernohrprothesen", BIOMEDIZINISCHE TECHNIK, Vol.34, No.7/8, pages 168-176, July/August 1989; XP000050246
 - D5: George C R: "Cochlear implants: technology for the profoundly deaf", MEASUREMENT + CONTROL, Vol.26, No.9, November 1993; XP000416746
 - D6: US-A-5 549 658 (SHANNON et al.) 27 August 1996
- 2. The subject-matter of claims 1 and 30 does not involve an inventive step (cf. Rule 65(1)(2) PCT), and therefore does not satisfy the criterion set forth in Article 33(3) PCT.





EXAMINATION REPORT - SEPARATE SHEET

- Regarding claim 1: D1 discloses an analogue audio signal processor comprising a compressor, a tone control ("a frequency selective function") and an expander (see Figs.1-3 and the corresponding text), which use MOSFETs operating in weak inversion. Tone control is obtained by a cascaded lowpass filters as shown in Fig.3. That the output of the cascaded lowpass filters are subtracted to obtain a band-pass filtered signal is not explicitly disclosed in D1. To make bandpass filter by such a combination of lowpass filters is one of many known methods. Given the cascaded lowpass filters of D1, the skilled person would without exerting any inventive skill use such a combination rather than e.g. combine high- and lowpass filters.
- Regarding claim 30: D3 discloses a multichannel cochlear implant as claimed in claim 30 except for the fact that log-domain filters comprising MOS transistors operating in weak inversion are used (see e.g. Fig.1,7A,7B and 8, column 5, line 38 - column 7, line 3 and column 8, lines 25-50). Considering the known advantages of such log-domain filters (e.g. low power consumption and high dynamic range) it is obvious to use such filters as are known from D1 in the cochlear implant of D3 (see also PCT Guidelines 3-IV,A1(v)).
- Dependent claims 2-9,13-29 and 31-39 do not contain any features which, in 3. combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, the reasons being as follows:
 - Regarding claims 2,4,5 and 26: See D1, parts referred to above. It is noted that the use of compression amplifiers for hearing aids using MOS in the weak inversion mode is also known from D2 (see e.g. Fig.1 and page 4, line 27 page 5, line 28).
 - Regarding claim 3: The feature contained in the claim is merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, in order to solve the problem posed.
 - Regarding claim 6: The use of amplifiers to bring the amplitude of an electric signal to the desired level is standard practice.

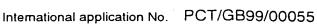
- Regarding claim 7: See D1, parts referred to above. It is noted that claim 3, to which claim 7 refers, implies the input signal is a voltage signal.
- Regarding claims 8,9,18-20 and 37-39: The use of full-wave rectifiers, biphase signal generators and interleave samplers as claimed in order to generate an output signal to be sent to the electrodes of a cochlear implant is known from D6 (see Figs.5-7, column 12, line 62 - column 15, line 36).
- Regarding claim 13: The mere choice for the number of outputs according to e.g. the intended application (hearing aid, single or multiple channel cochlear implant) does not involve any inventive activity.
- Regarding claim 14-16,21-25,31,36: See D3 parts referred to above.
- Regarding claim 17: See comments given above regarding claim 30.
- Regarding claims 32 and 35: The mere application of a remote control is obvious.
- Regarding claim 33 and 34: In-situ fitting and/or adjustment by the user is common practice.
- Regarding claims 27-29: The application of the claimed analogue audio processors in auditory prostheses, hearing aids, and cochlear implants plainly suitable for its new application is obvious (PCT Guidelines 3-IV,A1(v)).
- 4. Although the use of full-wave and half-wave rectifiers in processors for cochlear implants is known (see comments given above with respect to claim 9), none of the documents cited above disclose or hint at the specific arrangement as claimed in claim 10.
 - Claims 11 and 12 are dependent on claim 10 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

Re Item VII

Certain defects in the international application

1. The features of the claims are not provided with reference signs placed in parentheses (Rule 6.2(b) PCT).





EXAMINATION REPORT - SEPARATE SHEET

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art 2. disclosed in the documents D2-D6 are not mentioned in the description, nor are these documents identified therein.

25

23

CLAIMS

- An analogue audio signal processor, comprising an input for receiving an audio input signal, an output for providing a processed audio output signal, and a tone control circuit coupling the input to the output and comprising first and second log-domain filters having different low-pass bands and a subtractor for subtracting the output currents of the filters to produce a filtered signal, each of the filters comprising MOS transistors operating in weak inversion.
- 10 2. A processor according to claim 1, further comprising a compressor coupling the input to the tone control circuit for compressing the dynamic range of the input signal.
- 3. A processor according to claim 2, wherein the compressor is a voltage-tocurrent converter.
 - 4. A processor according to claim 2 or 3, wherein the compressor comprises MOS transistors operating in weak inversion.
- A processor according to claim 4, wherein the compressor is configured to provide control of sensitivity.
 - 6. A processor according to any of claims 1 to 5, further comprising an amplifier for amplifying the filtered output signal of the tone control circuit.
 - 7. A processor according to any of claims 1 to 6, wherein the input signal is a current signal.
- 8. A processor according to any of claims 1 to 7, further comprising a biphase signal generator for supplying to the output a biphase signal modulated by the processed audio output signal.



- 9. A processor according to any of claims 1 to 8, further comprising full-wave rectification means for full-wave rectifying the processed audio output signal.
- 10. A processor according to claim 9, wherein the tone control circuit further 5 comprises third and fourth filters having low-pass bands substantially identical to the first and second filters respectively and a further subtractor for subtracting the output currents of the third and fourth filters to produce a further filtered signal, and the full-wave rectification means comprises means coupled to the input for producing oppositely-phased audio signals from the 10 input signal, one of the oppositely-phased audio signals being supplied to the first and second filters and the other of the oppositely-phased audio signals being supplied to the third and fourth filters, half-wave rectification means for half-wave rectifying the filtered signals from the first-mentioned and further subtractors, and a combiner for combining the half-wave rectified signals to 15 effect full-wave rectification.
 - 11. A processor according to claim 10, wherein the third and fourth filters are log-domain filters comprising MOS transistors operating in weak inversion.
- 20 12. A processor according to claim 10 or 11, wherein the half-wave rectification means comprises means for applying a dc offset to the filtered signals.
 - 13. A processor according to any of claims 1 to 12, comprising only one output.
- A processor according to any of claims 1 to 12, comprising a plurality of outputs for providing processed audio signals, and wherein the tone control circuit is common to all the outputs for simultaneously adjusting the intensity/frequency of the processed audio signals at the outputs.
- A processor according to claim 14, further comprising frequency separation means for separating the intensity/frequency adjusted audio signal into a plurality of frequency-separated signals having different frequency bands.

25

- 16. A processor according to claim 15, wherein the frequency separation means comprises a plurality of band-pass filters.
- 5 17. A processor according to claim 16, wherein the band-pass filters are log-domain filters comprising MOS transistors operating in weak inversion.
 - 18. A processor according to any of claims 15 to 17, further comprising a plurality of biphase signal generators for supplying biphase signals modulated by respective ones of the frequency-separated signals to respective ones of the outputs.
- 19. A processor according to claim 18, further comprising sampling means for applying samples of the frequency-separated signals to the respective biphase signal generators.
 - 20. A processor according to claim 19, wherein the sampling means comprises a continuous interleaved sample generator.
- 20 21. A processor according to any of claims 1 to 20, where configured such that the intensity/frequency is controllable by a user.
 - 22. A processor according to claim 21, comprising means controllable by the user for adjusting the frequency response of the tone control circuit.
 - 23. A processor according to claim 22, comprising user controls for controlling bass cut/boost and treble cut/boost.
- 24. A processor according to any of claims 21 to 23, comprising a user control for controlling signal amplitude.



- 25. A processor according to any of claims 1 to 24, wherein the or each subtractor has a control input for controlling signal amplitude.
- A processor according to any of claims 1 to 25, when implemented as a single chip analogue MOS integrated circuit.
 - 27. An aural prosthetic device comprising the processor according to any of claims 1 to 26.
- 10 28. A hearing aid comprising the processor according to any of claims 1 to 26.
 - 29. A cochlear implant prosthesis comprising the processor according to any of claims 1 to 26.
- 15 30. A multi-channel analogue audio signal processor for use with a cochlear prosthesis, comprising:

an input for receiving an audio signal;

- a plurality of outputs for connection to respective ones of cochlear implant electrodes;
- a plurality of analogue signal processing channels coupled to the input, each channel comprising a log-domain filter comprising MOS transistors operating in weak inversion and being coupled to a respective one of the outputs; and
- adjustment means for adjusting the intensity/frequency response of each channel.
 - 31. A processor according to claim 30, wherein each channel further comprises an amplifier having controllable gain, the gain of which amplifier is adjustable by the adjustment means.
 - 32. A processor according to claim 30 or 31, wherein the adjustment means includes a control interface for allowing adjustment of the gain of each

20



channel in response to control signals transmitted by a wireless remote control.

- A processor according to any of claims 30 to 32, further comprising a tone generator for generating tones of preset amplitude and frequency dependent on the fundamental frequencies of the filters of the channels.
 - 34. A processor according to claim 33, further comprising tone generator control means for selecting the frequency of the tone produced by the tone generator.
 - 35. A processor according to claim 34, wherein the tone generator control means comprises a wireless remote control.
- 15 36. A processor according to any of claims 30 to 35, where configured such that each channel is adjustable independently of all the other channels.
 - A processor according to any of claims 30 to 36, further comprising sampling means coupling the channels to the outputs.
 - 38. A processor according to claim 37, wherein the sampling means comprises a continuous interleaved sample generator.
- 39. A processor according to any of claims 30 to 38, further comprising a plurality of biphase signal generators for supplying to the outputs biphase signals modulated by the output signals of the channels.



The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving office use only	
International App. on No.	
International Filing Date	
Name of receiving Office and "PCT International A	pplication"

Applicant's or agent's file reference P003839WO RWP (if desired) (12 characters maximum) Box No. I TITLE OF INVENTION **AUDIO SIGNAL PROCESSORS APPLICANT** Box No. II Name and address: (Family name followed by given name; for a legal entity, full official designation. The This person is also inventor. address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.) Telephone No. Imperial College of Science, Technology & Medicine Sherfield Building Facsimile No. **Exhibition Road** London SW7 2AZ Teleprinter No. United Kingdom State (i.e. country) of nationality: State (i.e. country) of residence: IJĸ This person is applicant for all designated all designated States except the the United States the States indicated in United States of America the purposes of: States the Supplemental Box of America only Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S) Name and address: (Family name followed by given name; for a legal entity, full official designation. The This person is: address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.) applicant only O'NEILL, Graham 15 Brynmorlais St √ applicant and inventor Penydarren Merthyr Tydfil inventor only (if this check-box is CF47 9YE marked, do not fill in below) United Kingdom State (i.e. country) of nationality: State (i.e. country) of residence: UK UK the United States This person is applicant for all designated States except the the States indicated in all designated the purposes of: the Supplemental Box States United States of America of America only Further applicant and/or (further) inventors are indicated on a continuation sheet AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE Box No. IV The person identified below is hereby/has been appointed to act on behalf of agent common representative the applicant(s) before the competent International Authorities as: (Family name followed by given name; for a legal entity, full official designation. Telephone No. Name and address: The address must include postal code and name of country.) +44 1703 634816 PRATT, Richard Wilson, et al Facsimile No. D Young & Co +44 1703 224262 21 New Fetter Lane London EC4A 1DA Teleprinter No. United Kingdom 477667 YOUNGS G Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

If none of the f Name and address: (Faminy name familiary) by the name, for a legal entity, full official designation. The address of the purposes of the purposes of the purposes of: Insurance of the purposes of the pu	Continuation of Box No. III FURTHER APPLICANTS	AND/OR (FURTHER	R) INVENTORS
address must michate pasted code and name of country. The country of the address indicated in this Box is mapplicant State (a. country) of mationality: GERNANOVIX, Walter Rus Plo XII 731 aglo. 1102 85020-311 Londrina Parana Brazil This person is applicant for all designated all designated States except the purposes of: This person is applicant for all designated below.) State (a. country) of nationality: BRAZIL This person is applicant for all designated below.) State (a. country) of nationality: This person is applicant for all designated below.) State (a. country) of nationality: This person is applicant for all designated below.) This person is applicant for all designated below.) State (a. country) of nationality: This person is applicant for all designated below.) State (a. country) of nationality: This person is applicant for all designated below. State (a. country) of nationality: This person is applicant for all designated below. State (a. country) of nationality: This person is applicant for all designated below. State (a. country) of nationality: This person is applicant for all designated below. State (a. country) of nationality: This person is applicant for all designated below. State (a. country) of nationality: This person is applicant for all designated all designated below. State (a. country) of nationality: This person is applicant for all designated all designated below. State (a. country) of nationality: State (a. country) of nationality: This person is applicant for all designated all designated below. State (a. country) of nationality: This person is applicant for all designated all designated below. State (a. country) of nationality: This person is applicant for all designated all designated below. State (a. country) of nationality: This person is applicant and inventor all designated all designated below. State (a. country) of nationality: This			
GERMANOVIX, Walter Rus Plo XII BRAZIL State (i.e. country) of nationality: BRAZIL This person is applicant for all designated below. Name and address: (Femily name followed by given name, for a legal entity, full official designation. The applicant and inventor inventor only (if this check-box is marked, do not fill in below) TOUMAZOU, Christopher 4 Hurst tal name Cumrod Hill OXX 29PR United Kingdom State (i.e. country) of nationality: UK State (i.e. country) of residence: What paplicant for all designated below. State (i.e. country) of residence: WK This person is applicant for all designated below. State (i.e. country) of nationality: UK This person is applicant for all designated below. State (i.e. country) of nationality: UK This person is applicant for all designated below. State (i.e. country) of nationality: UK This person is applicant for all designated below. State (i.e. country) of nationality: UK This person is applicant for all designated below. State (i.e. country) of nationality: UK This person is applicant for all designated below. State (i.e. country) of nationality: UK This person is applicant for all designated below. State (i.e. country) of nationality: UK This person is applicant for all designated below. State (i.e. country) of nationality: UK This person is applicant for all designated below. State (i.e. country) of nationality: This person is applicant only in the state indicated in the Box is the State indicated i	address must include postal code and name of country. The country of the address	s indicated in this Box is	This person is:
Rua Pio XII 731 aplo 1102 86020-311 Londrina Parana Brazil State (i.e. country) of nationality: BRAZIL State (i.e. country) of residence: BRAZIL State (i.e. country) of nationality: BRAZIL State (i.e. country) of nationality: BRAZIL State (i.e. country) of residence: BRAZIL State (i.e. country) of residence: BRAZIL This person is applicant for country name followed by given name, for a legal entity, full official designation. The applicant State (i.e. country) of residence in ordinate and inventor country. The country of his address indicated in this Box is marked, do not fill in below) TOUMAZOU, Christopher 4 Hurst tane Cunnor Hill Oxford OX2 9PR United Kingdom State (i.e. country) of nationality: UK State (i.e. country) of residence: UK This person is applicant for country of the address indicated with the supplemental Box Name and address. (Femily mane followed by given name, for a legal entity, full official designation. The marked, do not fill in below) State (i.e. country) of nationality: UK This person is applicant and inventor UK This person is applicant for country of the address indicated in this Box is the supplemental Box Name and address. (Femily mane followed by given name, for a legal entity, full official designation. The difference of the purposes of the supplemental Box State (i.e. country) of residence in ordinate of country. The country of the defices indicated in this Box is the applicant's State (i.e. country) of residence is indicated below.) State (i.e. country) of residence in ordinate of residence is indicated below.) State (i.e. country) of residence in ordinate of residence is indicated below.) This person is applicant only of nationality: State (i.e. country) of residence: This person is applicant only of residence in ordinate of residence is indicated below.) This person is applicant only of nationality: State (i.e. country) of residence: This person is applicant for country of residence is indicated to below.) This person is applicant and invent		20.0,	applicant only
State (i.e. country) of nationality: BRAZIL This person is applicant for all designated states except the proposes of: Inventor only if this check-box is marked, do not fill in below) BRAZIL This person is applicant for all designated states except the proposes of: Inventor only if this check-box is marked, do not fill in below) This person is applicant for all designated states except the proposes of: Inventor only if this check-box is marked, do not fill in below) ToUMAZOU, Christopher all the states of marked below. State (i.e. country) of nationality: State (i.e. country) of nationality: Inventor only if this check-box is marked, do not fill in below) State (i.e. country) of nationality: This person is applicant for all designated states except the proposes of: Inventor only if this check-box is marked, do not fill in below) State (i.e. country) of nationality: State (i.e. country) of residence is indicated below. State (i.e. country) of nationality: This person is applicant for all designated states except the proposes of characters and name of country. The country of the address indicated in this Box is marked, do not fill in below) State (i.e. country) of nationality: This person is applicant for all designated below. Inventor only (if his check-box is marked, do not fill in below) Name and address: (Family name followed by given name, for a legal entity, full directed designation. The marked, do not fill in below) State (i.e. country) of nationality: State (i.e. country) of nationality: This person is applicant for all designated below. Name and address: (Family name followed by given name, for a legal entity, full directed designation. The marked, do not fill in below) Name and address: (Family name followed by given name, for a legal entity, full directed designation. The marked, do not fill in below) Name and address: (Fam	Rua Pio XII		√ applicant and inventor
State (i.e. country) of nationality: BRAZIL This person is applicant for all designated all designated States except the the purposes of: all designated states all designated all designation. The states indicated in the States all designation all desig	86020-311 Londrina Parana		inventor only (if this check-box is
This person is applicant for all designated all desig	Brazii		marked, do not fill in below)
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The states indicated below.) ToUMAZOU, Christopher 4 Hurst Lane Cumnor Hill Oxford OX2 9PR United Kingdom State (i.e. country) of nationality: IX State (i.e. country) of nationality: IX State (i.e. country) of nationality: IX State (i.e. country) of residence: IX This person is applicant for all designated below.) Name and address: (Family name followed by given name; for a legal entity, full official designation. The address indicated in this Box is not address. (Family name followed by given name; for a legal entity, full official designation. The address indicated in this Box is not address. (Family name followed by given name; for a legal entity, full official designation. The address indicated in this Box is not address. (Family name followed by given name; for a legal entity, full official designation. The address indicated in this Box is not address. (Family name followed by given name; for a legal entity, full official designation. The address indicated in this Box is not address. (Family name followed by given name; for a legal entity, full official designation. The address indicated in this Box is not address. (Family name followed by given name; for a legal entity, full official designation. The address indicated in this Box is not applicant only if this check-box is marked, on not fill in below) State (i.e. country) of nationality: State (i.e. country) of nationality: This person is applicant for all designated legal entity, full official designation. The marked, on not fill in below) This person is applicant only (if this check-box is marked, do not fill in below) State (i.e. country) of nationality: This person is applicant for all designated legal entity, full official designation. The marked, do not fill in below) This person is applicant for all designated legal entity, full official designation. The marked, do not fill	State (i.e. country) of nationality: BRAZIL	State (i.e. country) of res	i . idence: BRAZIL
Name and address: (Family name followed by given name; for a legal entity, full efficial designation. The address must include postal code and name of country. The country) of residence: TOUMAZOU, Christopher 4 Hurst Lane Cumnor Hill Oxford OX2 9FR United Kingdom State (i.e. country) of nationality: It is person is applicant for state of unity state of unity states of America only if this check-box is marked, do not fill in below) Name and address: (Family name followed by given name; for a legal entity, full efficial designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant only of residence in the purposes of: State (i.e. country) of residence in oxidence if no State of residence is indicated below.) This person is applicant for address: (Family name followed by given name; for a legal entity, full efficial designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant only applicant and inventor This person is applicant for all designated all designated States except the one that the United States indicated in the Dunited States of America only of residence in the purposes of: State (i.e. country) of nationality: This person is applicant for all designated in this designation. The marked, do not fill in below) Name and address: (Family name followed by given name; for a legal entity, full designation. The marked, do not fill in below) This person is applicant only of nationality: This person is applicant only of nationality: This person is applicant for all designated in this designation. The marked, do not fill in below) State (i.e. country) of nationality: This person is applicant for all designated in this above the united States in dicated below.) This person is applicant for all designate	This person is applicant for	States except the	the United States the States indicated in
address must include postal code and name of country. The country of the address indicated below.) TOUMAZOU, Christopher 4 Hurst Lane Cumnor Hill Oxford OXA PR United Kingdom State (i.e. country) of nationality: UK State (i.e. country) of nationality: UK This person is applicant for all designated below.) States If any name followed by given name; for a legal entity, full official designation. The address indicated below.) State (i.e. country) of nationality: State (i.e. country) of nationality: State (i.e. country) of nationality: This person is applicant for below given name; for a legal entity, full official designation. The applicant's State (i.e. country) of residence: This person is applicant for below given name; for a legal entity, full official designation. The applicant's State (i.e. country) of residence if no State of residence is indicated below.) State (i.e. country) of nationality: This person is applicant for all designated below.) Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the States indicated in this Box is the supplicant only (if this check-box is marked, do not fill in below) Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the States indicated in this Box is the States indicated in this Box is marked, do not fill in below) State (i.e. country) of nationality: This person is applicant for all designated all designated all designated states except the the United States of America only of residence: This person is applicant for all designated all designated states except the the United States indicated in this Box is the States indicate		of America	
TOUMAZOU, Christopher 4 Hurst Lane Cumnor Hill Oxford OX2 9PR United Kingdom State (i.e. country) of nationality: UK State (i.e. country) of nationality: UK State (i.e. country) of nationality: UK State (i.e. country) of residence: UK This person is applicant for all designated by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.) State (i.e. country) of nationality: State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated below. Name and address: (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated below. Name and address: (i.e. country) of residence: This person is applicant for all designated below. Name and address: (i.e. country) of residence: This person is applicant for all designated below. Name and address: (i.e. country) of residence: This person is applicant for all designated below. State (i.e. country) of residence: This person is applicant for all designated below. State (i.e. country) of residence: This person is indicated below. State (i.e. country) of residence: This person is applicant only (if this check-box is marked, do not fill in below) State (i.e. country) of residence: This person is applicant only (if this check-box is marked, do not fill in below) State (i.e. country) of residence: This person is applicant only (if this check-box is marked, do not fill in below) State (i.e. country) of residence: This person is applicant for all designated all designated states except the the United States indicated in the fox is marked, do not fill in below) State (i.e. country) of residence: This person is applicant only (if this check-box is marked, do not fill in below)	address must include postal code and name of country. The country of the address	ss indicated in this Box is	This person is:
A Hurst Lane Cumor Hill Oxford OX2 9PR United Kingdom State (i.e. country) of nationality: UK State (i.e. country) of residence: UK This person is applicant for all designated bates of America Oxidenses must include postal code and name of country. The country of the address indicated in this Box is the applicant state (i.e. country) of residence: State (i.e. country) of nationality: This person is applicant and inventor I mixed on this in below) This person is: I applicant and inventor I inventor only (if this check-box is marked, do not fill in below) State (i.e. country) of nationality: This person is applicant for all designated bates of America only of residence: This person is applicant for bates of America only of residence: This person is applicant for all designated bates of America only inventor only (if this check-box is marked, do not fill in below) Name and address: (Family name followed by given name, for a legal entity, full official designation. Name and address: (Family name followed by given name, for a legal entity, full official designation. Name and address: (Family name followed by given name, for a legal entity, full official designation. Name and address: (Family name followed by given name, for a legal entity, full official designation. Name and address: (Family name followed by given name, for a legal entity, full official designation. The united States indicated in this Box is the State (i.e. country) of residence: I inventor only (if his check-box is marked, do not fill in below) State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated all designated ballow.)			applicant only
Oxford OX2 9PR United Kingdom State (i.e. country) of nationality: UK State (i.e. country) of residence: UK This person is applicant for all designated by given name, for a legal entity, full official designation. The applicant state (i.e. country) of residence is indicated in this Box is the applicant for all designated by given name. State of residence is indicated below.) State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated all designated States except the United States of America only if this check-box is marked, do not fill in below) State (i.e. country) of nationality: This person is applicant for all designated all designated States except the United States of America only if this check-box is marked, do not fill in below) Name and address: (Femily name followed by given name: for a legal entity, full official designation. The applicant states indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.) State (i.e. country) of nationality: State (i.e. country) of nationality: State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated all designated below.) Inventor only (if this check-box is marked, do not fill in below) This person is:	4 Hurst Lane		applicant and inventor
State (i.e. country) of nationality: UK State (i.e. country) of residence: UK This person is applicant for the purposes of: It all designated States except the purposes of: States I all designated States except the purposes of America only the States indicated in the Supplemental Box of America only the Supplemental Box of America only the States indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.) State (i.e. country) of nationality: This person is applicant for all designated and name of country. The address indicated his his Box is marked, do not fill in below) State (i.e. country) of nationality: This person is applicant for all designated and name of country of the address indicated below.) State (i.e. country) of nationality: This person is applicant for all designated and name of country of the address indicated in this Box is marked, do not fill in below)	Oxford		inventor only (if this check-box is
This person is applicant for the purposes of: All designated All designated All designated America America Internation Internat	- · · - ·	•	marked, do not fill in below)
the purposes of: States United States of America Of America only the Supplemental Box Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.) State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated States United States except the the United States the States indicated in the State of America only the States indicated in the State of America only the States indicated in the State of America only applicant only applicant only the States indicated in the States indicated in the State of America only applicant and inventor inventor only (if this check-box is marked, do not fill in below)	State (i.e. country) of nationality: UK	State (i.e. country) of res	.l. sidence: UK
address must include postal code and name of country. The country of the address indicated below.) State (i.e. country) of residence if no State of residence is indicated below.) State (i.e. country) of nationality: State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated below. States when the purposes of: United States of America only if this check-box is marked, do not fill in below) Name and address: (Femily name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.) State (i.e. country) of nationality: State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant and inventor inventor only (if this check-box is marked, do not fill in below) State (i.e. country) of nationality: This person is applicant for all designated all designated states except the the United States in the States indicated in the States indi	This person is applicant for all designated the purposes of:	States except the of America	the United States of America only the States indicated in the Supplemental Box
This person is applicant for States	address must include postal code and name of country. The country of the addre	ss indicated in this Box is	applicant only applicant and inventor
This person is applicant for States all designated States except the United States of America only the States indicated in the purposes of: Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.) State (i.e. country) of nationality: State (i.e. country) of nationality: State (i.e. country) of residence: the States indicated in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in the States indicated in this Box is I in the States indicated in the States indicated in this Box is I in the States indicated in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in this Box is I in the States indicated in the States indicated in this Box is I in the States indicated in the States indicated in the States indicated in this Box is I in the States indicated in the States indicated in the States in	State // a country of nationality	State (i.e. country) of res	Lsidence:
the purposes of: States United States of America Of America only the Supplemental Box Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.) This person is: This person is: applicant only if this check-box is marked, do not fill in below) State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated all designated all designated States except the the United States the States indicated in this Box is the States indica	State (i.e. country) of Haddinanty.		
address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.) applicant and inventor inventor only (if this check-box is marked, do not fill in below) State (i.e. country) of nationality: State (i.e. country) of residence: the United States the States indicated in this Box is		States except the of America	
the applicant's State (i.e. country) of residence if no State of residence is indicated below.) applicant only applicant and inventor applicant and inventor only (if this check-box is marked, do not fill in below) State (i.e. country) of residence: This person is applicant for all designated all designated States except the the United States the States indicated	Name and address: (Family name followed by given name; for a legal entity, I	full official designation. The	This person is:
State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated all designated States except the the United States the States indicated in the states in the states indicated in the states in the states indicated in the states in the states in the states indicated in the states in	address must include postal code and name or country. The country of the address the applicant's State (i.e. country) of residence if no State of residence is indicate.	d below.)	applicant only
State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated all designated States except the the United States the States indicated in the states in the states indicated in the states in the states indicated in the states in the states in the states indicated in the states in			applicant and inventor
State (i.e. country) of nationality: State (i.e. country) of residence: This person is applicant for all designated all designated States except the the United States indicated in the States and indicated in the States in the States indicated in the States in the States indicated in the States i	·		L 1
This person is applicant for all designated all designated States except the the United States the States indicated in			
Time person to opposit it. All designated and designated office of the state of th	State (i.e. country) of nationality:	State (i.e. country) of re	sidence:
Further applicants and/or (further) inventors are indicated on a continuation sheet	the purposes of: ! ! States !! United States	of America	

Further applicants and/or (further) inventors are indicated on a continuation Form PCT/RO/101 (continuation sheet) (January 1997; reprint January 1998)

See Notes to the request form

Box No. V	DESIGNATION OF STATES			
The following	designations are h made under Rule 4.9(a) (mark	the	applic	cable ch xes; at least one must be marked):
Regional Pate	ent			
₩ AP	ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, Zimbabwe, and any other State which is a Contractin			ho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW f the Harare Protocol and of the PCT
₩ EA	Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Be Russian Federation, TJ Tajikstan, TM Turkmenistan, Convention and of the PCT			G Kyrgyzstan, KZ Kazakstan, MD Republic of Moldova, RU other State which is a Contracting State of the Eurasian Patent
√ ∫ EP	ES Spain, FI Finland, FR France, GB United Kingdon	n, G	R Gr	land and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, eece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL hich is a Contracting State of the European Patent Convention
√ oa	Gabon, GN Guinea, ML Mali, MR Mauritania, NE Nig	jer, S T (if	SN Se any c	Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA enegal, TD Chad, TG Togo, and any other State which is a other kind of protection or treatment desired, please specify on dotte
	nt (if other kind of protection or treatment desired, specif			
M AL Alb	pania	\mathbf{V}	LT	Lithuania
57 AM Am	menia	W	LU	Luxembourg
AT AU	stria	57	LV	Latvia
	atrolia	الركا	MD	Penublic of Moldova
VI AU AU	stralia	[V.]	IVID	Republic of Moldova
√ AZ Aze	erbaijan	M)	MG	Madagascar
BA Bos	snia and Herzegovina	M	MK	The former Yugoslav Republic of Macedonia
₩ BB Bai	rbados			
I BG Bul	lgaria	57	MN	Mongolia
BR Bra	ngail			Malawi
(A) DIX DIS	azil			
BY Bel				Mexico
CA Ca	nada			Norway
TO CH AND	D LI Switzerland and Liechtenstein	$\overline{\mathbf{M}}$	NZ	New Zealand .
NO Ch	ina	5 /1	PL	Poland
CU Cu	ba		PT	Portugal
19 CZ CZ	ach Papublic	[7]	РΩ	Pomania
VI CZ CZ	ech Republic	×	RU.	Kollidild
DE Ge	rmany	M	ΚU	Russian Federation
[√] DK Dei	nmark		SD	Sudan
√ EE Est	tonia	M	SE	Sweden
F ES Spa	ain	5 /1	SG	Singapore
√ FI Fin	nland	$\widetilde{\mathbf{M}}$	SI	Slovenia
	ited Kingdom		SK.	Slovakia
☑ GE Ge	eorgia	M	SL	Sierra Leone
GH Gh			-	Tajikstan
☑ GM Ga	mbia	\mathbf{V}	TM	Turkmenistan
	inea-Bissau			Turkey
THU Hu	***************************************	Ñ	TT	Trinidad and Tobago
<u> </u>	Ionesia	H	LIA	Ukraine
<u> </u>				Unamb
<u>√</u> iL Isra				Uganda
☑ IS Ice	eland	\mathbf{V}	US	United States of America
JP Jap	pan			
√ KE Kei	nya	\mathbb{Z}	UZ	Uzbekistan
KG Kry	yqyzstan	K/	VN	Viet Nam
KP De	ygyzstan mocratic People's Republic of Korea	H	YH	Yunoslavia
ו (ענותר טפו	modalio r copie a Nepublio di Notea	씱	71/	Yugosiavia Zimbabwe
		S.		
KR Re	public of Korea	CI	neck-	boxes reserved for designating States (for the purposes of a
∐√ KZ Kaa	zakstan	na		I patent) which have become party to the PCT after the
√ LC Sai	int Lucia	is	suano	ce of this sheet:
T LK Sri			HR	Croatia
TO LR Lib		پي		
===		씯		
LS Les	sotho	M	IN	India
l e				

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

			Sheet No	0. 4		
Box No. VI	PRIORITY	M .		Further prior	ns are indicated in the	e Supplemental Box
The priority of the	following earlier	application(s) is here	eby claimed:			
	intry lich, the application filed)	Filing D (day/mon		Application I	No. (onl	Office of filing ly for regional or international application)
item (1) United	d Kingdom	12 Jan 1	1998	9800585.3	3	
item (2) United	d Kingdom	27 Jul 1	1998	9816351.2	2	
item (3)						
is the receiving O	office (a fee may b	be required):				present international application
SV Bureau a cer	rtified copy of the) identified above	e as item(s): (1) and (2	2)	
Box No. VII		ONAL SEARCHIN				
Choice of Internat competent to carry	tional Searching A	Authority (ISA) (If two al search, indicate the	or more Internal Authority chosen;	tional Searching Author the two-letter code may t	rities are be used): ISA / EP	0
Earlier Search Fill in the Authority is now i	where a search (into	temational, international the international search, (I-type or other) by the to the extent possib	he International Search A	uthority has already bee arlier search. Identify s	en carried out or requested and uch search or request either by
Country (or region		•	day/month/year)	Glorido de dise e e e	Number:	
Box No. VII	CHECK LIST	T			•	·
This international following number	al application con er of sheets:	itains the	This internation	nal application is accomp	panied by the item(s)	marked below:
1. request	: 4	sheets	1. separate attorney	te signed power of	5. 🚺 fee calculat	tion sheet
2. description		sheets		general power of		dications concerning
3. claims	: 9	sheets	stateme	yent explaining lack of	nucleotide a	nicroorganisms and/or amino acid
4. abstract	: 1	sheets	3. Signatur	ге		isting (diskette)
5. drawings	: 12	sheets		documents(s) ed in Box No. VI as	8. other (speci	ify):
Tot	tal : 48	sheets				
Figure No. 2	of the d	Irawings (if any) shou	uld accompany th	ne abstract when it is pu	ıblished	
Box No. IX		OF APPLICANT				
Next to each sign	ature, indicate th	ne name of the pers	on signing and t	the capacity in which t	he person signs (if s	such capacity is not obviou
F	'RATT, Rich	hard Wilson				
1 Date of actua	al receipt of the po	urnorted	For receiving C	Office use only		
international	application:	·				2. Drawings:
timely receive		ipt due to later but wings completing oplication:				received:
	y receipt of the re inder PCT Article					not received:
	Searching Authorthe applicant:	ority ISA /		6. Transmittal o until search fo	f search copy delayedee paid	d
Data of receipt (-f the record con		For International	Bureau use only		
the International	of the record copy	/ by				

\X\(\rightarrow\)

PATENT COOPERATION TREATY







INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

P003839W0 RWP	FOR FURTHER see Notification o (Form PCT/ISA/	f Transmittal of International Search Report 220) as well as, where applicable, item 5 below.
International application No.	International filing date(day month year)	(Exchine) Priority Date (day/month/year)
PCT/GB 99/00055	08 January 1999 (08.01.99)	12 January 1998 (12.01.98)
Applicant		
IMPERIAL COLLEGE OF SCIENC	CE, TECHNOLOGY & MEDICINE	et al.
This international search report has been according to Article 18. A copy is being to	prepared by this International Searching Authors ansmitted to the International Bureau.	ority and is transmitted to the applicant
This international search report consists o X It is also accompanied by a copy	f a total of 2 sheets. of each prior art document cited in this repo	r i.
1. Certain claims were found unsear	chable (see Box I).	
2. Unity of invention is lacking (see	Box II).	
3. The international application con international search was carried o	tains disclosure of a nucleotide and/or amino s out on the basis of the sequence listing	acid sequence listing and the
[liled	with the international application.	
[Curnis	shed by the applicant separately from the inte	rnational application,
<u>.</u> L_	but not accompanied by a statement to the matter going beyond the disclosure in the	e effect that it did not include international application as filed.
Trans	cribed by this Authority	
<u> </u>	xt is approved as submitted by the applicant	
the te	xt has been established by this Authority to r	read as follows:
5. With regard to the abstract,		
the tex	ct is approved as submitted by the applicant thas been established, according to Rule 38. It. The applicant may, within one month from report, submit comments to this Authority.	m the date of mailing of this international
	, a resemble to this reducity.	•
6. The figure of the drawings to be publish	ed with the abstract is:	
	gested by the applicant.	None of the figures.
	e the applicant failed to suggest a figure.	
because	e this figure better characterizes the inventio	n.
DOM DOTIES THE A		

Form PCT/ISA/210 (first sheet) (July 1992)

Ing	onal Application No PCT/GB	99/0005
_		

INTERNATIONAL SEARCH REPO	onal Application No PCT/GB 99
OF SUBJECT MATTER	

 Λ.	CLASSIFICATION	OF	SUBJECT	MATTER
Λ.	CLASSIFICATION	OF	SUBJECT	MATTER

H 04 R 25/00

According to International Patent Classification (IPC) or to both national classification and IPC6

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

H 04 R,H 04 B,A 61 N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5276739 A (KROKSTAD et al.) 04 January 1994 (04.01.94), Abstract, column 1, line 5 - column 4, line 2, fig. 1,5, claim 1.	1,11, 22,47, 50
A	US 5549658 A (SHANNON et al.) 27 August 1996 (27.08.96), abstract, column 1, line 5 - column 5, line 50, fig. 1, claim 1.	1,11, 22,47, 50
A	US 4993073 A	

Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
Special categories of cited documents: A document defining the general state of the art which is not considered to be of particular relevance E earlier document but published on or after the international filing date L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) O document referring to an oral disclosure, use, exhibition or other means P document published prior to the international filing date but later than the priority date claimed Date of the actual completion of the international search 21 April 1999	To later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family Date of mailing of the international search report 2 8, 05, 1999
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016 Form PCT/ISA/210 (second sheet) (July 1992)	Authorized officer GRÖSSING e.h.

ANHANG

ANNEX

ANNEXE

zum internationalen Recherchen-bericht über die internationale Patentanmeldung Nr.

to the International Search Report to the International Patent Application No.

au rapport de recherche inter-national relatif à la demande de brevet international n°

PCT/GB 99/00055 SAE 219543

In diesem Anhang sind die Mitglieder der Patentfamilien der im obenge- members relating to the patent documents nannten internationalen Recherchenbericht angeführten Patentdokumente angegeben. Diese Angaben dienen nur zur Unter- richtung und erfolgen ohne Gewähr.

This Annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The Office is in no way liable for these particulars which are given merely for the purpose of information.

La presente annexe indique les membres de la famille de brevets relatifs aux documents de brevets cités dans le rapport de recherche international visée ci-dessus. Les reseignements fournis sont donnés à titre indicatif et n'engagent pas la responsibilité de l'Office.

Im Recherchenbericht angeführtes Patentdokument Patent document cited in search report Document de brevet cité dans le rapport de recherche		Datum der Veröffentlichung Publication date Date de publication	Mitglied(er) der Pafentfamilie Patent family member(s) Membre(s) de la famille de brevets		Datum der Veröffentlichung Publication date Date de publication	
US A	5276739	04-01-1994	SZZZZLITTTMMMUUUUVVV CCCCCHHWTUXMMMCCH MARCHABHACHAMMOU MARCHAMMOO	79688777740012700885 64/25000054444700885 15422222000544447968 166005550992 5889111 8 99 2 9 5	99999999999999999999999999999999999999	
US A	5549658	27-08-1996	AU A1 WO A1 US A	38899795 9612456 5749912	15-05-1976 02-05-1976 12-05-1998	
US A.	4993073	12-02-1991	EP A2 A20 EP B A00 EG B B A00 EG B B A00	310456 8730251 8730252 88210535 22210535 8723086	05-04-1989 05-12-1990 03-02-1988 09-11-1988 07-04-1989 04-12-1991 04-11-1987	